

10/798773

=> d his

(FILE 'HOME' ENTERED AT 09:20:04 ON 29 MAR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,  
LIFESCI' ENTERED AT 09:20:30 ON 29 MAR 2005

L1 1300316 S KINASE?  
L2 484232 S HUMAN AND L1  
L3 6994149 S CLON? OR EXPRESS? OR RECOMBINANT  
L4 241821 S L2 AND L3  
L5 6109328 S CARCINOMA OR BRAIN OR PITUITARY OR KIDNEY  
L6 2104477 S TRACHEA OR LUNG OR SALIVARY OR PROSTATE  
L7 637019 S UMBILICAL (A)VEIN OR AORTA OR ESOPHAGUS OR TONGUE  
L8 55574 S L4 AND L5  
L9 6103 S L4 AND L7  
E YU X/AU  
L10 2286 S E3  
E XIE Q/AU  
L11 709 S E3  
E ABUIN A/AU  
L12 182 S E3-E5  
E WALKE D W/AU  
L13 127 S E3-E6  
L14 3280 S L10 OR L11 OR L12 OR L13  
L15 117 S L4 AND L14  
L16 43 DUP REM L15 (74 DUPLICATES REMOVED)

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NEWS 2 "Ask CAS" for self-help around the clock  
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NEWS 4 FEB 28 PATDPAFULL - New display fields provide for legal status data from INPADOC  
NEWS 5 FEB 28 BABS - Current-awareness alerts (SDIs) available  
NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded  
NEWS 7 MAR 02 GBFULL: New full-text patent database on STN  
NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced  
NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER reloaded  
NEWS 10 MAR 22 KOREPAT now updated monthly; patent information enhanced  
NEWS 11 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY  
NEWS 12 MAR 22 PATDPASPC - New patent database available  
NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags  
  
NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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|            |   |
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FILE 'HOME' ENTERED AT 09:20:04 ON 29 MAR 2005

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 09:20:30 ON 29 MAR 2005

FILE 'EMBASE' ENTERED AT 09:20:30 ON 29 MAR 2005

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FILE 'LIFESCI' ENTERED AT 09:20:30 ON 29 MAR 2005  
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=> s kinase?

L1 1300316 KINASE?

=> s human and l1

7 FILES SEARCHED...

L2 484232 HUMAN AND L1

=> s clon? or express? or recombinant

4 FILES SEARCHED...

L3 6994149 CLON? OR EXPRESS? OR RECOMBINANT

=> s l2 and l3

L4 241821 L2 AND L3

=> s carcinoma or brain or pituitary or kidney

L5 6109328 CARCINOMA OR BRAIN OR PITUITARY OR KIDNEY

=> s trachea or lung or salivary or prostate

L6 2104477 TRACHEA OR LUNG OR SALIVARY OR PROSTATE

=> s umbilical (a)vein or aorta or esophagus or tongue

L7 637019 UMBILICAL (A) VEIN OR AORTA OR ESOPHAGUS OR TONGUE

=> s hypothalamus or ovary or uterus or placenta

COMMAND INTERRUPTED

If this message appears repeatedly, please notify the Help Desk.

Enter "HELP STN" for information on contacting the nearest STN Help Desk by telephone or via SEND in the STNMAIL file.

=> s l4 and l5

L8 55574 L4 AND L5

=> s l4 and l6

COMMAND INTERRUPTED

If this message appears repeatedly, please notify the Help Desk.

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=> sd his  
SD IS NOT A RECOGNIZED COMMAND  
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> d his

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L7 637019 S UMBILICAL (A)VEIN OR AORTA OR ESOPHAGUS OR TONGUE  
L8 55574 S L4 AND L5

=> s l4 and l7

L9 6103 L4 AND L7

=> s human (3w) 11

COMMAND INTERRUPTED

If this message appears repeatedly, please notify the Help Desk.  
Enter "HELP STN" for information on contacting the nearest STN Help  
Desk by telephone or via SEND in the STNMAIL file.

=> s l7 or l8

COMMAND INTERRUPTED

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L8 55574 S L4 AND L5  
L9 6103 S L4 AND L7

=> e yu x/au

E1 2 YU WYATT/AU  
E2 1 YU WZ/AU  
E3 2286 --> YU X/AU  
E4 1 YU X \*/AU  
E5 21 YU X A/AU  
E6 1 YU X A D/AU  
E7 237 YU X B/AU  
E8 199 YU X C/AU  
E9 7 YU X CHRISTOPHER/AU  
E10 144 YU X D/AU

E11 2 YU X D W/AU  
E12 5 YU X E/AU

=> s e3  
L10 2286 "YU X"/AU

=> e xie q/au  
E1 1 XIE PULING/AU  
E2 1 XIE PUTI/AU  
E3 709 --> XIE Q/AU  
E4 4 XIE Q A/AU  
E5 49 XIE Q B/AU  
E6 15 XIE Q C/AU  
E7 1 XIE Q C K C/AU  
E8 1 XIE Q CH/AU  
E9 17 XIE Q D/AU  
E10 34 XIE Q F/AU  
E11 14 XIE Q G/AU  
E12 63 XIE Q H/AU

=> s e3  
L11 709 "XIE Q"/AU

=> e abuin a/au  
E1 1 ABUIKA KUSIAK ALEKSANDRA/AU  
E2 1 ABUIKMIEL A/AU  
E3 71 --> ABUIN A/AU  
E4 2 ABUIN A S/AU  
E5 109 ABUIN ALEJANDRO/AU  
E6 3 ABUIN B C/AU  
E7 4 ABUIN C F/AU  
E8 1 ABUIN C FRANCO/AU  
E9 3 ABUIN C M F/AU  
E10 1 ABUIN C M FRANCO/AU  
E11 1 ABUIN CABEZ L M/AU  
E12 2 ABUIN CABEZA L M/AU

=> s e3-e5  
L12 182 ("ABUIN A"/AU OR "ABUIN A S"/AU OR "ABUIN ALEJANDRO"/AU)

=> e walke d w/au  
E1 1 WALKE D/AU  
E2 2 WALKE D G/AU  
E3 62 --> WALKE D W/AU  
E4 62 WALKE D WADE/AU  
E5 2 WALKE DANIEL W/AU  
E6 1 WALKE DANIEL WADE/AU  
E7 1 WALKE E F/AU  
E8 4 WALKE E N/AU  
E9 1 WALKE E W/AU  
E10 3 WALKE ERIK N/AU  
E11 1 WALKE FRED/AU  
E12 1 WALKE G/AU

=> s e3-e6  
L13 127 ("WALKE D W"/AU OR "WALKE D WADE"/AU OR "WALKE DANIEL W"/AU OR "WALKE DANIEL WADE"/AU)

=> d his

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E XIE Q/AU  
L11 709 S E3  
E ABUIN A/AU  
L12 182 S E3-E5  
E WALKE D W/AU  
L13 127 S E3-E6

=> s 110 or 111 or 112 or 113  
L14 3280 L10 OR L11 OR L12 OR L13

=> s 14 and 114  
L15 117 L4 AND L14

=> dup rem 115  
PROCESSING COMPLETED FOR L15  
L16 43 DUP REM L15 (74 DUPLICATES REMOVED)

=> d 1-43 ibib ab

L16 ANSWER 1 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 1  
ACCESSION NUMBER: 2005-05163 BIOTECHDS  
TITLE: New isolated novel **human kinase** (NHK)  
nucleic acid and polypeptide, useful for diagnosing, drug  
screening, clinical trial monitoring, or treating diseases  
and disorders;  
recombinant enzyme protein production and  
antagonist and agonist for use in for gene therapy  
AUTHOR: HU Y; WILGANOWSKI N L; FRIDDLE C J; WALKE D W  
PATENT ASSIGNEE: LEXICON GENETICS INC  
PATENT INFO: US 6841377 11 Jan 2005  
APPLICATION INFO: US 2002-171374 13 Jun 2002  
PRIORITY INFO: US 2002-171374 13 Jun 2002; US 2001-297856 13 Jun 2001  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2005-072303 [08]

AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule (I) comprises a nucleotide sequence that encodes a sequence comprising 359 amino acids (SEQ ID NO. 2), or hybridizes under stringent conditions to the nucleotide sequence comprising 1080 bp (SEQ ID NO. 1) or its complement, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a **recombinant expression** vector comprising an isolated nucleic acid molecule comprising SEQ ID NO. 1; and (2) a host cell comprising the vector of (1).

WIDER DISCLOSURE - Also disclosed as new are: (1) agonists and antagonists of NHK; and (2) identifying compounds that modulate NHK **expression** and/or NHK activity.

BIOTECHNOLOGY - Preferred **Expression** Vector: In the **recombinant expression** vector, the isolated nucleic acid molecule encodes the amino acid sequence of SEQ ID NO. 2. Preferred

Host Cell: The host cell is prokaryotic or eukaryotic. Preferably, the cell is a yeast cell, an insect cell, an animal cell, or a mammalian cell.

USE - The nucleic acid and polypeptide sequences are useful for the identification of coding sequence and mapping a unique gene to a particular chromosome. They can also be used for diagnosis, drug screening, clinical trial monitoring, treatment of diseases and disorders, and in cosmetic or nutriceutical applications.

EXAMPLE - No example given. (14 pages)

L16 ANSWER 2 OF 43 HCPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2005:151237 HCPLUS  
DOCUMENT NUMBER: 142:235493  
TITLE: Protein and cDNA sequences of novel **human** protein **kinase** homologs  
INVENTOR(S): **Walke, D. Wade**; Hilbun, Erin; Donoho, Gregory; Turner, C. Alexander, Jr.; Hansen, Gwenn; Beltranelrio, Hector; Van Sligtenhorst, Isaac  
PATENT ASSIGNEE(S): Lexicon Genetics Incorporated, USA  
SOURCE: U.S., 31 pp., Cont.-in-part of U.S. Ser. No. 854,856.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 6858419             | B1   | 20050222 | US 2001-10720   | 20011113    |
| US 6541252             | B1   | 20030401 | US 2001-854856  | 20010514    |
| PRIORITY APPLN. INFO.: |      |          | US 2000-206015P | P 20000519  |
|                        |      |          | US 2001-854856  | A2 20010514 |

AB The present invention relates to the discovery, identification, and characterization of nucleotides that encode novel **human** proteins, and the corresponding amino acid sequences of these proteins. The novel **human** proteins (NHPs) described for the first time herein, collectively referred to herein as ENZ66 (ENZ66 is also referred to as WNK1), share structural similarity with animal **kinases**, including, but not limited to, mitogen activated protein (MAP) **kinases**, serine/threonine protein **kinases**, P21-activated protein **kinases**, and NPK1-related protein **kinases**. As such, the novel polynucleotides encode novel **kinases** having homologues and orthologs across a range of phyla and species.

REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD.. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 2

ACCESSION NUMBER: 2004-23078 BIOTECHDS  
TITLE: New isolated nucleic acid molecule encoding a protein **kinase**, and the encoded enzyme, useful e.g. in diagnostics and in drug screening; vector-mediated protein-**kinase** gene transfer and **expression** in host cell for **recombinant** protein production and drug screening

AUTHOR: **WALKE D W; SCOVILLE J; FRIDDLE C J**  
PATENT ASSIGNEE: **WALKE D W; SCOVILLE J; FRIDDLE C J**  
PATENT INFO: US 2004175749 9 Sep 2004  
APPLICATION INFO: US 2004-803278 18 Mar 2004  
PRIORITY INFO: US 2004-803278 18 Mar 2004; US 2001-293248 24 May 2001  
DOCUMENT TYPE: Patent  
LANGUAGE: English

OTHER SOURCE: WPI: 2004-652024 [63]

AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule comprising a sequence of 1449 bp (SEQ ID NO: 3) fully defined in the specification, a sequence that encodes an amino acid sequence comprising 482 amino acids (SEQ ID NO: 4) also given in the specification, or a sequence that encodes SEQ ID NO: 4 and hybridizes under stringent conditions to the complement of SEQ ID NO: 3, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a substantially isolated protein having the **kinase** activity of the protein in SEQ ID NO: 4 which is encoded by a nucleotide sequence that hybridizes to SEQ ID NO: 3 under highly stringent conditions.

WIDER DISCLOSURE - Disclosed are processes for identifying compounds that modulate **expression** and/or activity of the protein above.

USE - The polynucleotide or the encoded protein is useful for identifying compounds that modulate **expression** and/or activity of the protein, such modulator can be used in the diagnosis, drug screening, clinical trial monitoring, the treatment of diseases and disorders, and cosmetic or nutriceutical applications. The polynucleotide is useful as DNA markers for restriction fragment length polymorphism analysis, and in forensic biology. The sequences are useful for mapping and identifying the coding regions of the **human** genome, and for defining exon splice junctions. The protein is useful for generating antibodies, as reagents in diagnostic assays, for identifying other cellular gene products related to a **human** protein above, and as reagents in assays for screening for compounds that can be used as pharmaceutical reagents useful in the therapeutic treatment of mental, biological or medical disorders and diseases.

EXAMPLE - None given. (17 pages)

L16 ANSWER 4 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 3

ACCESSION NUMBER: 2004-24720 BIOTECHDS

TITLE: New nucleic acids encoding **human kinase** proteins, useful for identifying protein coding sequences and mapping a unique gene to a particular chromosome, or as additional DNA markers for restriction fragment length polymorphism analysis;

**recombinant** protein production via plasmid **expression** in host cell for use in chromosome mapping and forensics

AUTHOR: WALKE D W; SCOVILLE J; FRIDDLE C J

PATENT ASSIGNEE: LEXICON GENETICS INC

PATENT INFO: US 6797510 28 Sep 2004

APPLICATION INFO: US 2002-196927 20 May 2002

PRIORITY INFO: US 2002-196927 20 May 2002; US 2001-293248 24 May 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2004-687770 [67]

AB DERWENT ABSTRACT:

NOVELTY - A new isolated nucleic acid molecule comprises a sequence of 1449 bp (SEQ ID NO: 3) given in the specification, or encodes a 482-amino acid sequence (SEQ ID NO: 4) also given in the specification.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a **recombinant expression** vector comprising a nucleic acid encoding SEQ ID NO: 4; and (2) a host cell comprising the **recombinant expression** vector.

WIDER DISCLOSURE - Also disclosed are the following: (1) agonists and antagonists of the novel **human** proteins (NHPs); (2) antibodies and nucleotide sequences that can be used to inhibit the **expression** of the NHPs; (3) transgenic animals that **express** NHP sequence; and (4) identifying compounds that modulate NHP **expression** and/or activity.

BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid comprised in the **expression** vector comprises SEQ ID NO: 3.

USE - The NHP sequences are useful for identifying protein coding sequences and mapping a unique gene to a particular chromosome, as additional DNA markers for restriction fragment length polymorphism analysis, or in forensic biology, particularly given the presence of nucleotide polymorphisms within the described sequences. (17 pages)

L16 ANSWER 5 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2004-20835 BIOTECHDS  
TITLE: New lentiviral vector comprising a cDNA encoding Hes1 polypeptide, useful treating cancer, disease caused by a pathogen, or neurological disorders, e.g. neurodegenerative disease, Huntington's disease, Guillain-Barre syndrome, or stroke;  
a **recombinant** lenti virus vector with a Hes-1 coding region and a reporter gene useful for disease gene therapy  
AUTHOR: CIVIN C I; YU X  
PATENT ASSIGNEE: UNIV JOHNS HOPKINS SCHOOL MEDICINE  
PATENT INFO: WO 2004072264 26 Aug 2004  
APPLICATION INFO: WO 2004-US4085 12 Feb 2004  
PRIORITY INFO: US 2003-498739 28 Aug 2003; US 2003-446939 12 Feb 2003  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2004-625865 [60]

AB DERWENT ABSTRACT:

NOVELTY - A lentiviral vector comprising a cDNA encoding Hes1 polypeptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a modified CD34+ hematopoietic stem cell (HSC) comprising the vector; (2) a method for promoting monocyte-macrophage cell, dendritic cell, or neural cell differentiation; (3) a composition comprising a monocyte-macrophage, dendritic cell, or neural cell produced by the method of (2), siRNA comprising the sequence gaaagatagc tcgcggcat SEQ ID NO: 21), antisense RNA comprising a sequence of 45 bp (SEQ ID NO: 24), and a physiological carrier; (4) a method of promoting pathogen immunity or cancer immunity; (5) an assay for evaluating whether a compound is an antagonist or an agonist of Hes1; and (6) a composition comprising siRNA comprising the sequence gaaagatagc tcgcggcat SEQ ID NO: 21), or an antisense RNA comprising a sequence of 45 bp (SEQ ID NO: 24).

BIOTECHNOLOGY - Preferred Vector: The vector further comprises a cDNA insertion site. The insertion site is occupied by a cDNA encoding a reporter gene, e.g. green or red fluorescent protein, chloramphenicol acetyltransferase or luciferase. The cDNA encoding Hes1 polypeptide and the cDNA encoding the reporter gene are transcribed from separate promoters. Preferred Modified CD34+ HSC: The cell is isolated from bone marrow, umbilical cord blood, mobilized peripheral blood or nonmobilized peripheral blood. Preferred Composition: The carrier is an isotonic solution, biocompatible matrix or gel. Preferred Method: Promoting monocyte-macrophage cell, dendritic cell, or neural cell differentiation comprises modifying a CD34+ HSC to decrease or increase **expression** of a Hes1 polypeptide and culturing the modified CD34+ HSC in monocyte-macrophage, dendritic cell, or neural cell differentiation promoting conditions until a monocyte-macrophage, dendritic cell, or neural cell phenotype emerges. The monocyte-macrophage differentiation promoting conditions comprise incubating the HSCs with Kit ligand, thrombopoietin (TPO), Frms-like tyrosine kinase-3 (FLT3), granulocyte-monocyte colony stimulating factor (GM-CSF), interleukin-2 (IL-2) and erythropoietin (Epo). The dendritic cell differentiation promoting conditions comprise incubating the HSCs with TPO, FLT3, Kit ligand, GM-CSF, and IL-4. The neural cell differentiation promoting conditions comprise incubating HSCs with nerve growth factor or

brain-derived growth factor. The neural cell differentiation promoting conditions comprise incubating HSCs with basic fibroblast growth factor, platelet-derived growth factor or epidermal growth factor. The CD34+ HSC stem cell is a mammalian CD34+ HSC or a **human** CD34+ HSC. The macrophage-monocyte phenotype comprises CD14, CD45, CD13 or CD33 cell surface markers. The dendritic cell phenotype comprises presence of HLA-DR and CD1a cell surface markers and absence of CD14 cell surface marker. The neural cell phenotype comprises presence of neuron-specific enolase. The neural cell phenotype comprises presence of oligodendrocyte marker 4 or glial fibrillary marker 4. The Hes1 is decreased by contacting a CD34+ HSC with Hes-1 siRNA of SEQ ID NO: 21 or with a Hes-1 antisense RNA of SEQ ID NO: 24. Promoting pathogen immunity or cancer immunity comprises administering the composition of (3) to a subject. Preferred Assay: An assay for evaluating whether a compound is an antagonist or an agonist of Hes1 comprises culturing cells containing the lentiviral vector and assaying for evidence of transcription of the reporter gene in the cells. The cells are mammalian cells. The assay comprises assaying for mRNA transcribed from the reporter gene. The assay comprises assaying for induction of transcription of the reporter gene in the cells. The reporter gene is contained in a reporter plasmid, where the non-endogenous DNA which **expresses** the Hes1 protein(s) or its functional modified forms is contained in an **expression** plasmid, where the reporter gene and **expression** plasmids also contain a selectable marker. The reporter gene is operatively linked to a Hes1 response element, i.e. PU.1 promoter. The cells are HSCs or neural stem cells.

ACTIVITY - Cytostatic; Virucide; Antimicrobial; Antiparasitic; Antibacterial; Antihelminthic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Nootropic; Antiinflammatory; CNS-Gen; Cerebroprotective; Vasotropic. No biological data given.

MECHANISM OF ACTION - Gene Therapy.

USE - The vector, modified HSC, composition, and method are useful treating malignancies, inborn errors of metabolism, hemoglobinopathies, immunodeficiencies, cancer, disease caused by a pathogen, e.g. virus, parasites, bacteria, or helminths, neurological disorders like neurodegenerative disease, neurotrauma, Parkinson's disease, Huntington's disease, multiple sclerosis, Alzheimer's disease, amyotrophic lateral sclerosis, Guillain-Barre syndrome, or stroke. (73 pages)

L16 ANSWER 6 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
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DUPLICATE 4

ACCESSION NUMBER: 2004467298 EMBASE

TITLE: RNA interference reveals that ligand-independent met activity is required for tumor cell signaling and survival.

AUTHOR: Shinomiya N.; Chong F.G.; **Xie Q.**; Gustafson M.; Waters D.J.; Zhang Y.-W.; Vande Woude G.F.

CORPORATE SOURCE: G.F. Vande Woude, Laboratory of Molecular Oncology, Van Andel Research Institute, Grand Rapids, MI 49503, United States. george.vandewoude@vai.org

SOURCE: Cancer Research, (1 Nov 2004) 64/21 (7962-7970).  
Refs: 50

ISSN: 0008-5472 CODEN: CNREA8

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology  
016 Cancer  
030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Hepatocyte growth factor/scatter factor-Met signaling has been implicated in tumor growth, invasion, and metastasis. Suppression of this signaling

pathway by targeting the Met protein tyrosine kinase may be an ideal strategy for suppressing malignant tumor growth. Using RNA interference technology and adenovirus vectors carrying small-interfering RNA constructs (Ad Met small-interfering RNA) directed against mouse, canine, and human Met, we can knock down c-met mRNA. We show a dramatic dependence on Met in both ligand-dependent and ligand-independent mouse, canine, and human tumor cell lines. Mouse mammary tumor (DA3) cells and Met-transformed NIH3T3 (M114) cells, as well as both human and canine prostate cancer (PC-3 and TR6LM, human sarcoma (SK-LMS-1), glioblastoma (DBTRG), and gastric cancer (MKN45) cells, all display a dramatic reduction of Met expression after infection with Ad Met small-interfering RNA. In these cells, we observe suppression of tumor cell growth and viability in vitro as well as inhibition of hepatocyte growth factor/scatter factor-mediated scattering and invasion in vitro, whether Met activation was ligand dependent or not. Importantly, Ad Met small-interfering RNA led to apoptotic cell death in many of the tumor cell lines, especially DA3 and MKN45, but did not adversely affect MDCK canine kidney cells. Met small-interfering RNA also abrogated downstream Met signaling to molecules such as Akt and p44/42 mitogen-activated protein kinase. We further show that intratumoral infection with c-met small-interfering RNA adenovirus results in a substantial reduction in tumor growth. Thus, Met small-interfering RNA adenoviruses are reliable tools for studying Met function and raise the possibility of their application for cancer therapy.

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on STN

DUPLICATE 5

ACCESSION NUMBER: 2004510339 EMBASE  
TITLE: Insulin-like growth factor-I regulation of hepatic scavenger receptor class BI.  
AUTHOR: Cao W.M.; Murao K.; Imachi H.; Yu X.; Dobashi H.; Yoshida K.; Muraoka T.; Kotsuna N.; Nagao S.; Wong N.C.W.; Ishida T.  
CORPORATE SOURCE: Dr. K. Murao, First Dept. of Internal Medicine, Faculty of Medicine, Kagawa University, 1750-1, Miki-cho, Kita-gun, Kagawa 761-0793, Japan. mkoji@kms.ac.jp  
SOURCE: Endocrinology, (2004) 145/12 (5540-5547).  
Refs: 49  
ISSN: 0013-7227 CODEN: ENDOAO  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 003 Endocrinology  
029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB High-density lipoprotein mediates a normal physiological process called reverse cholesterol transport. This process enables the transfer of cholesterol from peripheral tissues to the liver for further metabolism and eventual secretion in the form of bile. The scavenger receptor of the B class (SR-BI), human homolog of SR-BI, and CD36 and LIMP-II analogous-1 (CLA-1) are different names for the same receptor that facilitates hepatocellular uptake of cholesterol from high-density lipoprotein. The pivotal role of this receptor in enterohepatic circulation of cholesterol and bile salts underlies our interest to study the regulation of hepatic SR-BI gene in response to the actions of IGF-I. The results of our studies showed that endogenous expression of SA-BI/CLA-1 was suppressed by exposure to GH or IGF-I in cultured HepG2 cells. This observation extended to a whole animal model of rats continuously infused with IGF-I. IGF-I decreased transcriptional activity of the SR-BI promoter. However, the inhibitory effect of IGF-I on SR-BI/CLA-1 promoter activity was abrogated by wortmannin, a specific inhibitor of phosphoinositide 3-kinase (PI3-K). Exposure of HepG2 cells to IGF-I elicited a rapid phosphorylation of Akt. We also

demonstrated that the constitutively active form of both p110, a subunit of PI3-K, and Akt inhibited activity of the **human** SR-BI/CLA-1 promoter. Furthermore, the dominant-negative mutant of Akt abolished the ability of IGF-I to suppress activity of the SR-BI/CLA-1 promoter. In conclusion, PI3-K/Akt pathways participate in IGF-I-suppression of SR-BI/CLA-1 **expression**, which suggests that the activation of Akt plays an important role in cholesterol metabolism in liver.

L16 ANSWER 8 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

ACCESSION NUMBER: 2004307695 EMBASE  
TITLE: Transformation potency of ErbB heterodimer signaling is determined by B-Raf **kinase**.  
AUTHOR: Hatakeyama M.; Yumoto N.; **Yu X.**; Shirouzu M.; Yokoyama S.; Konagaya A.  
CORPORATE SOURCE: M. Hatakeyama, Bioinformatics Group, RIKEN Genomic Sciences Center, 1-7-22 Suehiro-cho, Yokohama, Kanagawa 230-0045, Japan. marikoh@gsc.riken.jp  
SOURCE: Oncogene, (24 Jun 2004) 23/29 (5023-5031).  
Refs: 45  
ISSN: 0950-9232 CODEN: ONCNES  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Cellular transformation occurs only in cells that **express** both ErbB1 and ErbB4 receptors, but not in cells **expressing** only one or the other of these receptors. However, when both receptors are coexpressed and ligand-stimulated, they interact with virtually the same adaptor/effector proteins as when **expressed** singly. To reveal the underlying regulatory mechanism of the **kinase**/phosphatase network in ErbB homo- and heterodimer receptor signaling, extracellular signal-regulated **kinase** (ERK) and Akt activities were evaluated in the presence of several enzyme inhibitors in ligand-induced cells **expressing** ErbB1 (E1), ErbB4 (E4), and ErbB1/ErbB4 (E1/4) receptor. The PP2A inhibitor okadaic acid showed receptor-specific inhibitory profiles for ERK and Akt activities. Moreover, B-Raf isolated only from E1/4 cells could induce in vitro phosphorylation for MEK; this B-Raf **kinase** activity was abolished by pretreatment of the cells with okadaic acid. Our study further showed that the E1/4 cell-specific B-Raf activity was stimulated by PLC $\gamma$  and subsequent Rap1 activation. The present study suggests that B-Raf **kinase**, which was specifically activated in the cells coexpressing ErbB1 and ErbB4 receptors, elevates total ERK activity within the cell and, therefore, can induce cellular transformation.

L16 ANSWER 9 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:292880 HCAPLUS  
DOCUMENT NUMBER: 141:361182

TITLE: **Wnk1 kinase** deficiency lowers blood pressure in mice: A gene-trap screen to identify potential targets for therapeutic intervention. [Erratum to document cited in CA140:106021]  
AUTHOR(S): Zambrowicz, Brian P.; **Abuin, Alejandro**; Ramirez-Solis, Ramiro; Richter, Elizabeth J.; Piggott, James; BeltrandelRio, Hector; Buxton, Eric C.; Edwards, Joel; Finch, Rick A.; Friddle, Carl J.; Gupta, Anupma; Hansen, Gwenn; Hu, Yi; Huang, Wenhua; Jaing, Crystal; Key, Billie Wayne, Jr.; Kipp, Peter; Kohlhauff, Buckley; Ma, Zhi-Qing; Markesich, Diane; Payne, Robert; Potter, David G.; Qian, Ny; Shaw, Joseph; Schrick, Jeff; Shi, Zheng-Zheng; Sparks, Mary

Jean; Van Sligtenhorst, Isaac; Vogel, Peter; Walke, Wade; Xu, Nianhua; Zhu, Qichao; Person, Christophe; Sands, Arthur T.  
CORPORATE SOURCE: Lexicon Genetics, The Woodlands, TX, 77381, USA  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2004), 101(12), 4332  
CODEN: PNASA6; ISSN: 0027-8424  
PUBLISHER: National Academy of Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The software used to generate the original graph depicting historical progression of estimated genome coverage by Omnibank failed to consistently select the earliest Omnibank sequence tag (OST) match to the sentinel gene list. Therefore, the rate of genome coverage is significantly greater in the initial phases of gene trap **clone** collection than that originally presented in the graph for Figure 2B. The corrected graph accurately illustrates an initial high rate of growth in genome coverage that then slows more significantly in the later stages of **clone** collection. The conclusions regarding total genomic coverage achieved by this methodol. as well as other aspects of the work are unchanged. The corrected figure and its legend are given.

L16 ANSWER 10 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN DUPLICATE 6

ACCESSION NUMBER: 2004088683 EMBASE  
TITLE: A Mutant High-Density Lipoprotein Receptor Inhibits Proliferation of **Human** Breast Cancer Cells.  
AUTHOR: Cao W.M.; Murao K.; Imachi H.; **Yu X.**; Abe H.; Yamauchi A.; Niimi M.; Miyauchi A.; Wong N.C.W.; Ishida T.  
CORPORATE SOURCE: K. Murao, First Dept. of Internal Medicine, Kagawa Medical University, 1750-1 Miki-cho, Kita-gun, Kagawa, Japan.  
mkoji@kms.ac.jp  
SOURCE: Cancer Research, (15 Feb 2004) 64/4 (1515-1521).  
Refs: 33  
ISSN: 0008-5472 CODEN: CNREA8  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 016 Cancer  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB High-density lipoprotein (HDL) stimulates the growth of many types of cells, including those of breast cancer. High levels of HDL are associated with an increased risk of breast cancer development. A scavenger receptor of the B class (SR-BI)/**human** homolog of SR-BI, CD36, and LIMPPII analogous-1 (CLA-1) facilitates the cellular uptake of cholesterol from HDL and thus augments cell growth. Furthermore, HDL is also believed to have antiapoptotic effects on various cell types, and this feature adds to its ability to promote cell growth. These collaborative roles of HDL and CLA-1 prompted us to assess the function of these components on **human** breast cancer cells. In this study, we created a mutant CLA-1 (mCLA) that lacked the COOH-terminal tail to determine its potential role in breast cancer cell growth. **Expression** of mCLA inhibited the proliferation of breast cancer cell line MCF-7. This inhibitory action of mCLA required the transcriptional factor activator protein-1 (AP-1), and the mutant receptor also affected the antiapoptotic features of HDL. The effect of HDL on AP-1 activation and [(3)H]thymidine incorporation was abrogated by wortmannin, a specific inhibitor of phosphoinositide 3-**kinase**. Furthermore, the dominant negative mutant of Akt abolished the ability of HDL to activate AP-1. These findings raise the possibility that the inhibitors of the effects of HDL may be of therapeutic value for breast cancer.

L16 ANSWER 11 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on

STN  
ACCESSION NUMBER: 2005:23438 BIOSIS  
DOCUMENT NUMBER: PREV200500022740  
TITLE: Development of glucose intolerance in male transgenic mice overexpressing **human** glycogen synthase **kinase-3beta** on a muscle-specific promoter.  
AUTHOR(S): Pearce, Nigel J. [Reprint Author]; Arch, Jonathan R. S.; Clapham, John C.; Coghlan, Matthew P.; Corcoran, Stacey L.; Lister, Carolyn A.; Llano, Andrea; Moore, Gary B.; Murphy, Gregory J.; Smith, Stephen A.; Taylor, Colleen M.; Yates, John W.; Morrison, Alastair D.; Harper, Alexander J.; Roxbee-Cox, Lynne; **Abuin, Alejandro**; Wargent, Ed; Holder, Julie C.  
CORPORATE SOURCE: Dept Vasc Biol, GlaxoSmithKline, New Fontiers Sci Pk-S, 3rd Ave, Harlow, Essex, CM19 5AW, UK  
SOURCE: Metabolism Clinical and Experimental, (October 2004) Vol. 53, No. 10, pp. 1322-1330. print.  
ISSN: 0026-0495 (ISSN print).  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 29 Dec 2004  
Last Updated on STN: 29 Dec 2004  
AB Glycogen synthase **kinase-3** (GSK-3) protein levels and activity are elevated in skeletal muscle in type 2 diabetes, and inversely correlated with both glycogen synthase activity and insulin-stimulated glucose disposal. To explore this relationship, we have produced transgenic mice that overexpress **human** GSK-3beta in skeletal muscle. GSK-3beta transgenic mice were heavier, by up to 20% ( $P < .001$ ), than their age-matched controls due to an increase in fat mass. The male GSK-3beta transgenic mice had significantly raised plasma insulin levels and by 24 weeks of age became glucose-intolerant as determined by a 50% increase in the area under their oral glucose tolerance curve ( $P < .001$ ). They were also hyperlipidemic with significantly raised serum cholesterol (+90%), nonesterified fatty acids (NEFAs) (+55%), and triglycerides (+00%). At 29 weeks of age, GSK-3beta protein levels were 5-fold higher, and glycogen synthase activation (-27%), glycogen levels (-58%) and insulin receptor substrate-1 (IRS-1) protein levels (-67%) were significantly reduced in skeletal muscle. Hepatic glycogen levels were significantly increased 4-fold. Female GSK-3beta transgenic mice did not develop glucose intolerance despite 7-fold overexpression of GSK-3beta protein and a 20% reduction in glycogen synthase activation in skeletal muscle. However, plasma NEFAs and muscle IRS-1 protein levels were unchanged in females. We conclude that overexpression of **human** GSK-3beta in skeletal muscle of male mice resulted in impaired glucose tolerance despite raised insulin levels, consistent with the possibility that elevated levels of GSK-3 in type 2 diabetes are partly responsible for insulin resistance. Copyright 2004 Elsevier Inc. All rights reserved.

L16 ANSWER 12 OF 43 MEDLINE on STN DUPLICATE 7  
ACCESSION NUMBER: 2004247144 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 15024403  
TITLE: Improved glucose homeostasis in mice overexpressing **human** UCP3: a role for AMP-kinase?  
AUTHOR: Schrauwen P; Hardie D G; Roorda B; Clapham J C; **Abuin A**; Thomason-Hughes M; Green K; Frederik P M; Hesselink M K C  
CORPORATE SOURCE: Department of Human Biology, Maastricht University, The Netherlands.. p.schrauwen@hb.unimaas.nl  
SOURCE: International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity, (2004 Jun) 28 (6) 824-8.  
Journal code: 9313169. ISSN: 0307-0565.

PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200409  
ENTRY DATE: Entered STN: 20040518  
Last Updated on STN: 20040928  
Entered Medline: 20040927

AB OBJECTIVE: An unexplained phenotype of mice overexpressing **human UCP3** is their improved glucose homeostasis. Since overexpression of UCP3 might affect the energy charge of the cell, we investigated whether these mice have an increased AMP-activated protein **kinase** (AMPK) activity. METHODS: Mitochondrial localisation of UCP3 was determined by immunoelectronmicroscopy and AMPK activity was measured in medial gastrocnemius of control mice and mice overexpressing **human UCP3**. RESULTS: Mice overexpressing **human UCP3** had 5.8 fold higher levels of UCP3 protein, for which mitochondrial localisation was confirmed by immunoelectronmicroscopy. The ATP/AMP ratio was significantly lower in mice over-expressing UCP3 compared to the wild-type (10.9+/-1.6 vs 20.4+/-1.9 AU, P=0.03). Over-expression of UCP3 resulted in increased AMPK alpha1 activity (1.23+/-0.05 vs 1.00+/-0.06 normalized values, P=0.004) and a tendency towards increased AMPK alpha2 activity (1.18+/-0.08 vs 1.00+/-0.10 normalized values, P=0.08). CONCLUSION: Increased AMPK activity provides a plausible explanation for the improved glucose tolerance characteristic for these mice.

L16 ANSWER 13 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2004-04631 BIOTECHDS

TITLE: New **human kinase** nucleic acid molecules, useful for diagnosis, drug screening, clinical trial monitoring and treating diseases or disorders associated with biological disorders or imbalances; involving vector-mediated gene transfer and expression in host cell for use in gene therapy  
AUTHOR: HU Y; NEPOMNICHY B; GERHARDT B; WALKE D W; FRIDDLE C J  
PATENT ASSIGNEE: HU Y; NEPOMNICHY B; GERHARDT B; WALKE D W; FRIDDLE C J  
PATENT INFO: US 2003175949 18 Sep 2003  
APPLICATION INFO: US 2003-430797 6 May 2003  
PRIORITY INFO: US 2003-430797 6 May 2003; US 2000-243893 27 Oct 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-898545 [82]

AB DERWENT ABSTRACT:  
NOVELTY - An isolated nucleic acid molecule comprising a sequence of 2829 (S1) or 927 (S2) bp, fully defined in the specification, is new.  
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for an isolated nucleic acid expression vector comprising a promoter element operatively positioned to express a transcript encoding a sequence of 942 or 308 amino acids, fully defined in the specification.

BIOTECHNOLOGY - Preferred Molecule: The nucleic acid molecule encodes a sequence of 942 or 308 amino acids, fully defined in the specification. It hybridizes under stringent conditions to S1 or its complement.

ACTIVITY - None given.

MECHANISM OF ACTION - Gene therapy.

USE - The nucleic acid molecules are useful for diagnosis, drug screening, clinical trial monitoring and treating diseases or disorders associated with biological disorders or imbalances. (17 pages)

L16 ANSWER 14 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2003-23467 BIOTECHDS

TITLE: New nucleic acid molecules encoding novel **human** proteins (NHPs), e.g. sharing sequence similarity with animal **kinases** or receptor tyrosine **kinases**, useful for diagnosis, drug screening, and treatment of diseases and disorders;

virus vector-mediated gene transfer and **expression** in bacterium, yeast, fungus, insect, mammal cell for **recombinant** protein-tyrosine-**kinase** receptor

AUTHOR: HU Y; NEPOMNICHY B; GERHARDT B; WALKE D W; FRIDDLE C J

PATENT ASSIGNEE: LEXICON GENETICS INC

PATENT INFO: US 6586230 1 Jul 2003

APPLICATION INFO: US 2001-4542 23 Oct 2001

PRIORITY INFO: US 2001-4542 23 Oct 2001; US 2000-243893 27 Oct 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-634547 [60]

AB DERWENT ABSTRACT:

NOVELTY - An isolated **human** nucleic acid molecule, comprising a sequence of 2829 or 927 base pairs (bp), or encodes a sequence of 942 amino acids, fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) an isolated nucleic acid **expression** vector comprising the nucleic acid molecule; and (2) a host cell comprising the **expression** vector.

WIDER DISCLOSURE - Also disclosed as new are: (1) encoded proteins, fusion proteins, polypeptides and peptides; (2) antibodies to the encoded proteins; (3) genetically engineered animals that either lack or over **express** the disclosed genes; (4) antagonist or agonist of proteins, including small molecules, large molecules; (5) mutant NHPs and other compounds that modulate the **expression** or activity of the proteins; and (6) transgenic animals that **express** a NHP sequence or knock-outs that do not **express** a functional NHP.

BIOTECHNOLOGY - Preparation: NHP gene homologs can be isolated from nucleic acid from an organism of interest by performing polymerase chain reaction (PCR) using two degenerate or wobble oligonucleotide primer pools designed on the basis of amino acid sequences. The PCR product can be subcloned and sequenced to ensure that the amplified sequences represent the sequence of the desired NHP gene. The PCR fragment can then be used to isolate a full length cDNA **clone** by a variety of methods. For example, the amplified fragment can be labeled and used to screen a cDNA library, such as a bacteriophage cDNA library. A cDNA encoding a mutant NHP sequence can be isolated, for example, by using PCR. In this case, the first cDNA strand may be synthesized by hybridizing an oligo-dT oligonucleotide to mRNA isolated from tissue known or suspected to be **expressed** in an individual putatively carrying a mutant NHP allele, and by extending the new strand with reverse transcriptase. Preferred Host: Escherichia coli, bacillus subtilis, Saccharomyces, Pichia, insect cell, Chinese hamster ovary, baby hamster kidney, 293 cell, 3T3 cell. Preferred Vector: Baculo virus, cauliflower mosaic virus, tobacco mosaic virus.

ACTIVITY - Neuroprotective; Nootropic.

MECHANISM OF ACTION - Gene therapy; **Human** protein (Anta)gonist; Antisense therapy. No biological data given.

USE - The nucleic acid molecules are useful for diagnosis, drug screening, clinical trial monitoring, the treatment of biological disorders, imbalances disorder and mental disorders, and cosmetic and nutriceutical applications. The nucleic acid molecules are useful as hybridization probe, assessing gene **expression** pattern, polymorphisms identification, drug screening, and pharmacogenomics. NHP oligonucleotides can be used for molecular mutagenesis or evolution of protein, generation of antibodies as reagent in diagnostic assay,

identification of other cellular gene product related to a NHP as reagents in assays for screening for compound, chromosome mapping and gene therapy.

EXAMPLE - No example given. (17 pages)

L16 ANSWER 15 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:254176 HCAPLUS

DOCUMENT NUMBER: 138:283310

TITLE: Protein and cDNA sequences of a **human** protein **kinase**

INVENTOR(S): **Walke, D. Wade**; Hilbun, Erin; Donoho, Gregory; Turner, C. Alexander, Jr.

PATENT ASSIGNEE(S): Lexicon Genetics Incorporated, USA

SOURCE: U.S., 11 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 6541252             | B1   | 20030401 | US 2001-854856  | 20010514    |
| US 6858419             | B1   | 20050222 | US 2001-10720   | 20011113    |
| PRIORITY APPLN. INFO.: |      |          | US 2000-206015P | P 20000519  |
|                        |      |          | US 2001-854856  | A2 20010514 |

AB The invention provides protein and cDNA sequences of a **human** protein that has structural similarity with animal protein **kinases**. The invention further relates to the use of protein **kinase** in therapeutic, diagnostic, and pharmacogenomic applications.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 16 OF 43 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 2003571452 MEDLINE

DOCUMENT NUMBER: PubMed ID: 14610273

TITLE: **Wnk1 kinase** deficiency lowers blood pressure in mice: a gene-trap screen to identify potential targets for therapeutic intervention.

AUTHOR: Zambrowicz Brian P; **Abuin Alejandro**; Ramirez-Solis Ramiro; Richter Elizabeth J; Piggott James; BeltrandelRio Hector; Buxton Eric C; Edwards Joel; Finch Rick A; Friddle Carl J; Gupta Anupma; Hansen Gwenn; Hu Yi; Huang Wenhua; Jaing Crystal; Key Billie Wayne Jr; Kipp Peter; Kohlhauff Buckley; Ma Zhi-Qing; Markesich Diane; Payne Robert; Potter David G; Qian Ny; Shaw Joseph; Schrick Jeff; Shi Zheng-Zheng; Sparks Mary Jean; Van Sligtenhorst Isaac; Vogel Peter; **Walke Wade**; Xu Nianhua; Zhu Qichao; Person Christophe; Sands Arthur T

CORPORATE SOURCE: Lexicon Genetics, 8800 Technology Forest Place, The Woodlands, TX 77381, USA.. brian@lexgen.com

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2003 Nov 25) 100 (24) 14109-14. Electronic Publication: 2003-11-10. Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-CG472819; GENBANK-CG472820; GENBANK-CG472821; GENBANK-CG472822; GENBANK-CG472823; GENBANK-CG472824; GENBANK-CG472825; GENBANK-CG472826; GENBANK-CG472827; GENBANK-CG472828; GENBANK-CG472829; GENBANK-CG472830;











GENBANK-CG473776; GENBANK-CG473777; GENBANK-CG473778;  
GENBANK-CG473779; GENBANK-CG473780; GENBANK-CG473781;  
GENBANK-CG473782; GENBANK-CG473783; GENBANK-CG473784;  
GENBANK-CG473785; GENBANK-CG473786; GENBANK-CG473787;  
GENBANK-CG473788; GENBANK-CG473789; GENBANK-CG473790;  
GENBANK-CG473791; GENBANK-CG473792; GENBANK-CG473793;  
GENBANK-CG473794; GENBANK-CG473795; GENBANK-CG473796;  
GENBANK-CG473797; GENBANK-CG473798; GENBANK-CG473799;  
GENBANK-CG473800; GENBANK-CG473801; GENBANK-CG473802;  
GENBANK-CG473803; GENBANK-CG473804; GENBANK-CG473805;  
GENBANK-CG473806; GENBANK-CG473807; GENBANK-CG473808;  
GENBANK-CG473809; GENBANK-CG473810; GENBANK-CG473811;  
GENBANK-CG473812; GENBANK-CG473813; GENBANK-CG473814;  
GENBANK-CG473815; GENBANK-CG473816; GENBANK-CG473817;  
GENBANK-CG473818

ENTRY MONTH:

200402

ENTRY DATE:

Entered STN: 20031216

Last Updated on STN: 20040203

Entered Medline: 20040202

AB The availability of both the mouse and **human** genome sequences allows for the systematic discovery of **human** gene function through the use of the mouse as a model system. To accelerate the genetic determination of gene function, we have developed a sequence-tagged gene-trap library of >270,000 mouse embryonic stem cell **clones** representing mutations in approximately 60% of mammalian genes. Through the generation and phenotypic analysis of knockout mice from this resource, we are undertaking a functional screen to identify genes regulating physiological parameters such as blood pressure. As part of this screen, mice deficient for the *Wnk1* **kinase** gene were generated and analyzed. Genetic studies in **humans** have shown that large intronic deletions in *WNK1* lead to its overexpression and are responsible for pseudohypoaldosteronism type II, an autosomal dominant disorder characterized by hypertension, increased renal salt reabsorption, and impaired K<sup>+</sup> and H<sup>+</sup> excretion. Consistent with the **human** genetic studies, *Wnk1* heterozygous mice displayed a significant decrease in blood pressure. Mice homozygous for the *Wnk1* mutation died during embryonic development before day 13 of gestation. These results demonstrate that *Wnk1* is a regulator of blood pressure critical for development and illustrate the utility of a functional screen driven by a sequence-based mutagenesis approach.

L16 ANSWER 17 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2003263058 EMBASE

TITLE: Lentiviral vectors with two independent internal promoters transfer high-level **expression** of multiple transgenes to **human** hematopoietic stem-progenitor cells.

AUTHOR: Yu X.; Zhan X.; D'Costa J.; Tanavde V.M.; Ye Z.; Peng T.; Malehorn M.T.; Yang X.; Civin C.I.; Cheng L.

CORPORATE SOURCE: L. Cheng, Sidney Kimmel Comp. Cancer Center, Department of Oncology, Johns Hopkins Univ. Sch. of Medicine, 1650 Orleans Street, Baltimore, MD 21231, United States.

lcheng2@jhmi.edu

SOURCE: Molecular Therapy, (1 Jun 2003) 7/6 (827-838).

Refs: 40

ISSN: 1525-0016 CODEN: MTOHCK

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

022 Human Genetics

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Lentiviral vectors (LVs) offer several advantages over traditional oncoretroviral vectors. LVs efficiently transduce slowly dividing cells, including hematopoietic stem-progenitor cells (HSCs), resulting in stable gene transfer and **expression**. Additionally, recently developed self-inactivating (SIN) LVs allow promoter-specific transgene **expression**. For many gene transfer applications, transduction of more than one gene is needed. We obtained inconsistent results in our attempts to coexpress two transgenes linked by an internal ribosomal entry site (IRES) element in a single bicistronic LV transcript. In more than six bicistronic LVs we constructed containing a gene of interest followed by an IRES and the GFP reporter gene, GFP fluorescence was undetectable in transduced cells. We therefore investigated how to achieve consistent and efficient coexpression of two transgenes by LVs. In a SIN LV containing the elongation factor 1 $\alpha$  promoter, we included a second promoter from cytomegalovirus, the phosphoglycerate **kinase** gene, or the HLA-DR $\alpha$  gene. Using a single LV containing two constitutive promoters, we achieved strong and sustained **expression** of both transgenes in transduced engrafting CD34(+) HSCs and their progeny, as well as in other **human** cell types. Thus, such dual-promoter LVs can coexpress multiple transgenes efficiently in a single target cell and will enable many gene transfer applications.

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on STN

ACCESSION NUMBER: 2003387119 EMBASE  
TITLE: Effect of C-terminal truncations on MLK7 catalytic activity and JNK activation.  
AUTHOR: Yu X.; Bloem L.J.  
CORPORATE SOURCE: L.J. Bloem, Cardiovascular Discovery Research, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285, United States. L.Bloem@lilly.com  
SOURCE: Biochemical and Biophysical Research Communications, (17 Oct 2003) 310/2 (452-457).  
Refs: 25  
ISSN: 0006-291X CODEN: BBRCA  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 029 Clinical Biochemistry  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Mixed lineage **kinase** 7 (MLK7) is a MAPKKK with enriched **expression** in heart and skeletal muscle that functions to activate JNK and p38. The MLKs have several conserved domains, including a leucine zipper that in other family members mediates oligomerization critical for catalytic activity and JNK activation. Nested C-terminal deletion mutants of MLK7 from 436 to 286 as well as a mutant lacking only the leucine zipper (dellZ) were generated to determine the role of these domains in catalytic activity and JNK activation. Specific activity of MLK7366 was 75% full length while 436, 322, and dellZ retained approximately 25% and 286, 4% of the full-length catalytic function, demonstrating that the leucine zipper, while not absolutely necessary for catalytic activity, is required to reach full catalytic function of the enzyme. Co-transfection studies of JNK with the MLK7 mutants demonstrated full JNK activation with MLK7, 436, and dellZ, marginal activation for 1-400 or 1-366, and no activation for 1-322, demonstrating that the leucine zipper is not required for JNK activation and that sequence contained in C-terminal residue 322-436 is necessary for full pathway activation by MLK7.  
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L16 ANSWER 19 OF 43 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.  
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ACCESSION NUMBER: 2003184252 EMBASE  
TITLE: Expression of vascular endothelial growth factor

AUTHOR: and its receptors in the rhesus monkey (*Macaca mulatta*) endometrium and placenta during early pregnancy.  
Wang H.; Li Q.; Lin H.; **Yu X.**; Qian D.; Dai J.;  
Duan E.; Zhu C.

CORPORATE SOURCE: C. Zhu, Stt. Key Lab. of Repro. Biology, Institute of Zoology, Chinese Academy of Sciences, 19, ZhongGuanCun Road, Beijing 100080, China. zhuc@panda.ioz.ac.cn

SOURCE: Molecular Reproduction and Development, (1 Jun 2003) 65/2 (123-131).  
Refs: 39  
ISSN: 1040-452X CODEN: MREDEE

COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 010 Obstetrics and Gynecology  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Vascular endothelial growth factor (VEGF) is fundamental for development and maintenance of endometrial and placental vascular function during pregnancy. While there are a number of studies on VEGF in the **human** placenta, they are mostly restricted to late pregnancy. To further understand the role of VEGF in mediating angiogenesis during **human** early pregnancy, we employed a rhesus monkey early pregnancy model to study the temporal and spatial **expression** of VEGF and its receptors, fms-like tyrosine **kinase** (Flt)-1, and **kinase**-insert domain-containing receptor (KDR) mRNAs and proteins in the uteri on day 12, 18, and 26 of pregnancy using *in situ* hybridization, RT-PCR, and immunohistochemistry. VEGF mRNA had been identified in the luminal epithelium on day 12, in the glandular epithelium on day 12 and 18, and the highest **expression** was detected in the walls of some spiral arterioles adjacent to the implantation site on day 18, in the placental villi and in the fetal-maternal border on day 18 and 26. Besides, immunostaining of VEGF was detected in the placental villi and endometrial compartments including spiral arteries walls and the glandular epithelium. The localization of VEGF in the endothelium correlates with the presence of Flt-1 and KDR receptors on vascular structure. All the results above suggest that VEGF-VEGFR pairs were involved in the process of trophoblast invasion, maternal vascular transformation, and fetoplacental vascular differentiation and development during the rhesus monkey early pregnancy. **Expression** of VEGF, Flt-1, and KDR in the epithelial cells also hints some additionally functional roles of VEGF during early pregnancy.  
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L16 ANSWER 20 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:358389 BIOSIS  
DOCUMENT NUMBER: PREV200300358389  
TITLE: Camptothecin-induced apoptosis of SH-SY5Y neuroblastoma cells.  
AUTHOR(S): **Yu, X.** [Reprint Author]; Caltagarone, J.; Bowser, R.  
CORPORATE SOURCE: Department of Pathology, University of Pittsburgh Medical Center, 3500 Terrace St., BST-S, Pittsburgh, PA, 15261, USA  
xiy1@imap.pitt.edu; caltagar@up.awing.upmc.edu;  
bowser@np.awing.upmc.edu  
SOURCE: FASEB Journal, (March 2003) Vol. 17, No. 4-5, pp. Abstract No. 412.19. <http://www.fasebj.org/>. e-file.  
Meeting Info.: FASEB Meeting on Experimental Biology: Translating the Genome. San Diego, CA, USA. April 11-15, 2003. FASEB.  
ISSN: 0892-6638 (ISSN print).  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English  
ENTRY DATE: Entered STN: 6 Aug 2003  
Last Updated on STN: 6 Aug 2003  
AB Activation of the p53-induced DNA damage response mediates either apoptosis or G1 cell cycle arrest. DNA-damaging agent camptothecin activates signaling pathways that normally control cell cycle, and activation of the cell cycle proteins plays a key role in apoptosis versus cell cycle arrest. p53 regulates a cell cycle checkpoint via induction of the cyclin-CDK inhibitor p21, which is the key regulator in cell growth/cell response to DNA damage and the hallmark of G1 cell cycle arrest. We report that after DNA-damaging agent camptothecin was applied, p53 protein levels increased within 8 hrs in retinoid acid differentiated SH-SY5Y neuroblastoma cells and the Bax protein was rapidly cleaved as detected by western blot. Immunocytochemistry for Bax after treatment showed altered subcellular distribution, and this immunoreactivity co-localized with that of p53. The increased **expression** of p53 in the cells induced rapid but brief elevation of p21 and gradual down-regulation of CDK4 protein levels. The cell apoptotic activities were verified by Hoechst dye staining and by activation of Caspase-3 using western blot. Interestingly, the CDK4/6 inhibitor olomoucine protected cells from camptothecin-mediated apoptosis. Our studies suggest that p21 may serve as a critical checkpoint regulator for both apoptosis and cell cycle arrest in the p53-induced DNA damage pathway. Hence, camptothecin may induce cell death via activation of cell cycle proteins or DNA damage/repair pathways.

L16 ANSWER 21 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 9

ACCESSION NUMBER: 2003-08154 BIOTECHDS  
TITLE: New **human kinase** proteins and polynucleotides, useful for cosmetic and nutriceutical applications, drug screening, clinical trial monitoring, diagnosing or treating diseases associated with biological disorders or imbalances; vector-mediated gene transfer and **expression** in host cell for **recombinant** protein production and gene therapy

AUTHOR: YU X; XIE Q; ABUIN A;

WALKE D W

PATENT ASSIGNEE: LEXICON GENETICS INC

PATENT INFO: WO 2002090517 14 Nov 2002

APPLICATION INFO: WO 2002-US14669 8 May 2002

PRIORITY INFO: US 2001-289727 9 May 2001; US 2001-289727 9 May 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-103514 [09]

AB DERWENT ABSTRACT:

NOVELTY - A substantially isolated protein having the **kinase** activity of a protein comprising a fully defined sequence of 479 (S2) or 94 (S4) amino acids given in the specification, is new. The protein is encoded by a nucleotide sequence that hybridizes to a sequence of 1440 (S1) or 285 (S3) base pairs (bp) fully defined in the specification, under highly stringent conditions.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an isolated nucleic acid molecule comprising: (a) the sequence of S1 or S3; (b) a nucleotide sequence that encodes the amino acid sequence of S2, and hybridizes under stringent conditions to the nucleotide sequence of S1 or its complement; or (c) a nucleotide sequence encoding the amino acid sequence of S2 or S4.

WIDER DISCLOSURE - Also disclosed are host cell **expression** systems, fusion proteins, polypeptides and peptides, antibodies to the encoded proteins and peptides, genetically engineered animals that either lack or over **express** the polynucleotides, agonists and

antagonists of the proteins, and other compounds that modulate the expression or activity of the proteins encoded by the polynucleotides.

ACTIVITY - None given.

MECHANISM OF ACTION - **Kinase** Inhibitor; **Kinase** Stimulator; Gene Therapy.

USE - The polynucleotides, proteins, antibodies, agonists and antagonists of the proteins are useful for drug screening, clinical trial monitoring, and diagnosing or treating diseases or disorders associated with biological disorders or imbalances. The proteins and polynucleotides are also useful in cosmetic and nutriceutical applications, for identifying protein coding sequences and mapping a unique gene to a particular chromosome. The sequence of the polynucleotides and proteins can also be used as additional DNA markers for restriction fragment length polymorphism analysis, or in forensic biology.

EXAMPLE - No example given. (40 pages)

L16 ANSWER 22 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 10

ACCESSION NUMBER: 2002-19616 BIOTECHDS

TITLE: Novel nucleic acid molecule encoding a **human kinase**, useful in therapeutic, diagnostic and pharmacogenomic applications, as DNA markers for restriction fragment length polymorphism analysis and in forensic biology

;

**recombinant** enzyme protein and agonist and antagonist use in disease therapy and gene therapy

AUTHOR: **WALKE D W; MARICAR M; YU X; FRIDDLE C J**

PATENT ASSIGNEE: LEXICON GENETICS INC

PATENT INFO: WO 2002046428 13 Jun 2002

APPLICATION INFO: WO 2000-US48533 7 Dec 2000

PRIORITY INFO: US 2000-251941 7 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-527921 [56]

AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule (I) comprising a nucleotide sequence encoding a sequence (S1) of 424 amino acids fully defined in the specification, and hybridizes under stringent conditions to a sequence (S2) of 1275 nucleotides fully defined in the specification, or its complement, is new.

WIDER DISCLOSURE - Also disclosed are: (1) a host cell expression system **expressing** (I); (2) a protein encoded by (I); (3) a fusion protein comprising the protein encoded by (I); (4) antibodies or anti-idiotypic antibodies to the protein encoded by (I); (5) a genetically engineered animal that either lacks or overexpresses (I); (6) antagonists or agonists of the protein encoded by (I); (7) a compound that modulates the **expression** or activity of the protein encoded by (I); (8) a pharmaceutical formulation and method for treating biological disorders; (9) a protein that is functionally equivalent to the protein encoded by (I); and (10) a DNA vector that contains the **human kinase** coding sequences and/or their complements.

USE - (I) is useful in therapeutic, diagnostic and pharmacogenomic applications, and for identifying compounds that modulate, i.e., act as agonists or antagonists of the gene **expression** or gene product activity. (I) is useful for the identification of protein coding sequences, for mapping a unique gene to a particular chromosome, as additional DNA markers for restriction fragment length polymorphism (RFLP) analysis and in forensic biology, for screening libraries, isolating **clones**, preparing, **cloning** and sequencing templates, as hybridization probes, in microarrays or other assay formats, to screen collections of genetic material from patients who have

a particular medical condition, to identify mutations associated with a particular disease and also as a diagnostic or prognostic assay. (I) is useful for the detection of mutant **human** proteins, or inappropriately **expressed** proteins for the diagnosis of disease, for screening for drugs effective in the treatment of the symptomatic or phenotypic manifestations of perturbing the normal function of the protein in the body, for generation of antibodies, for identification of other cellular gene products related to the protein, and as reagents in assays for screening for compounds that can be used as pharmaceutical agents in the therapeutic treatment of mental, biological or medical disorders and diseases.

EXAMPLE - None given. (37 pages)

L16 ANSWER 23 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2003-06803 BIOTECHDS

TITLE: Novel **human** proteins that shares structural similarity with animal **kinases**, useful for therapeutic, diagnostic and pharmacogenomic applications; **recombinant** enzyme protein production and sense and antisense sequence for use in gene therapy

AUTHOR: YU X; MIRANDA M; FRIDDLE C J

PATENT ASSIGNEE: LEXICON GENETICS. INC

PATENT INFO: WO 2002081671 17 Oct 2002

APPLICATION INFO: WO 2002-US10787 4 Apr 2002

PRIORITY INFO: US 2001-282031 6 Apr 2001; US 2001-282031 6 Apr 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-058539 [05]

AB DERWENT ABSTRACT:

NOVELTY - An isolated novel **human** protein (NHP) (I) having the **kinase** activity of a protein (Ia) comprising a 385 residue amino acid sequence (S1), given in the specification, and encoded by a nucleotide sequence that hybridizes to a 1158 nucleotide sequence (S2), given in the specification under highly stringent conditions, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an isolated nucleic acid molecule (II) comprising S2 or its complement, and encoding S1.

WIDER DISCLOSURE - (1) agonists and antagonists of NHP, or other compounds that modulate the **expression** or activity of the protein; (2) host cell **expression** systems comprising (II); (3) fusion proteins comprising (I) that direct NHP to a target organ and/or facilitate transport across the membrane into the cytosol; (4) antibodies or anti-idiotypic antibodies specific to (I); (5) genetically engineered animals that either lack or overexpress (I); (6) antisense or ribozyme molecules, and open reading frames of regulatory sequence replacement constructs; (7) process for identifying compounds that modulate i.e. act as agonists or antagonists of NHP **expression** and/or NHP activity that use purified preparations of the NHP and/or NHP products, or cells **expressing** the above; and (8) proteins that are functionally equivalent to the NHP products encoded by (II).

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - (I) and (II) are useful for diagnosis, drug screening, clinical trial monitoring, the treatment of diseases and disorders, and cosmetic or nutriceutical applications. (II) is useful for the identification of protein coding sequences, and mapping a unique gene to a particular chromosome. (II) is also useful as an additional DNA marker for restriction fragment length polymorphism (RFLP) analysis and in forensic biology. (II) is useful in conjunction with the polymerase chain reaction (PCR) to screen libraries, to isolate **clones** and to prepare **cloning** and sequencing templates. (I) or (II) are useful for the detection of mutant NHPs or inappropriately **expressed** NHPs for the diagnosis of disease, and for screening

for drugs effective in the treatment of the symptomatic or phenotypic manifestations of perturbing the normal function of NHP in the body. NHP products are useful as therapeutics. NHP products are also useful for the generation of antibodies, as reagents in diagnostic assays, for the identification of other cellular gene products related to NHP, and as reagents in assays for screening compounds that can be used as pharmaceutical reagents useful in the therapeutic treatment of mental, biological or medical disorders and diseases.

EXAMPLE - None given. (39 pages)

L16 ANSWER 24 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2003-05423 BIOTECHDS

TITLE: **New human kinase** polynucleotides, useful for diagnosis, drug screening, clinical trial monitoring, treating mental, biological or medical disorders and diseases, and for cosmetic or nutriceutical applications; vector-mediated **recombinant** protein gene transfer and **expression** in host cell for use in drug screening, gene therapy and forensics

AUTHOR: YU X; MIRANDA M

PATENT ASSIGNEE: LEXICON GENETICS INC

PATENT INFO: WO 2002074932 26 Sep 2002

APPLICATION INFO: WO 2002-US8959 20 Mar 2002

PRIORITY INFO: US 2001-277168 20 Mar 2001; US 2001-277168 20 Mar 2001

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-759892 [82]

AB DERWENT ABSTRACT:

NOVELTY - A new isolated nucleic acid molecule comprises: (a) a sequence of 1368 base pairs fully defined in the specification; (b) a nucleotide sequence encoding a fully defined sequence of 455 amino acids given in the specification; or (c) a sequence that hybridizes under stringent conditions to the sequence of (a) or its complement.

WIDER DISCLOSURE - Also disclosed are: (1) agonists and antagonists of the polypeptides encoded by the polynucleotides; (2) transgenic animals that **express** the polypeptides which are useful for the *in vivo* study, testing and validation of **human** drug targets; (3) host cells **expressing** the nucleotides; (4) DNA vectors comprising the polynucleotides; and (5) antibodies that specifically recognize one or more epitopes of the polypeptides.

BIOTECHNOLOGY - Preparation: The polynucleotides can be synthesized by standard methods, such as the use of an automated DNA synthesizer.

ACTIVITY - Neuroleptic.

MECHANISM OF ACTION - **Kinase** Inhibitor; **Kinase** Stimulator; Gene Therapy.

USE - The **human kinase** polynucleotides are useful for diagnosis, drug screening, clinical trial monitoring, treating diseases and disorders, and cosmetic or nutriceutical applications. They are also useful as additional DNA markers for restriction fragment length polymorphism analysis and in forensic biology. The polynucleotides can also be used for generating antibodies, as reagents in diagnostic assays, or as reagents in assays for screening for compounds that can be used as pharmaceutical reagents useful in the therapeutic treatment of mental, biological or medical disorders and diseases.

ADMINISTRATION - No administration routes or dosage details given.

EXAMPLE - No example given. (37 pages)

L16 ANSWER 25 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2003-01894 BIOTECHDS

TITLE: Novel polynucleotide encoding **human** proteins that are structurally similar to animal **kinases**, useful for drug screening, diagnosis, in gene therapy of disorders and diseases e.g. cancer and pharmacogenomic applications;

**recombinant** enzyme protein production and sense  
and antisense sequence use in disease therapy and gene  
therapy

AUTHOR: **YU X; MIRANDA M; FRIDDLE C J**

PATENT ASSIGNEE: LEXICON GENETICS INC

PATENT INFO: WO 2002059325 1 Aug 2002

APPLICATION INFO: WO 2001-US50497 20 Dec 2001

PRIORITY INFO: US 2000-258335 27 Dec 2000; US 2000-258335 27 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-599796 [64]

AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule (I) comprising a nucleotide sequence encoding a novel **human** protein (NHP) of 2054 (S1) or 1958 (S2) amino acids given in specification, that share structural similarity with animal **kinases**, including serine-threonine **kinases**, particularly Citron rho-interacting **kinases**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule (II) comprising a nucleotide sequence that encodes (S1) and hybridizes under stringent conditions to a sequence (S3) of 6165 base pairs given in the specification, or its complement; and (2) an isolated nucleic acid molecule (III) comprising at least 24 contiguous bases of (S3).

WIDER DISCLOSURE - Disclosed are: (1) novel **human** proteins (NHPs) encoded by (I), that share structural similarity with animal **kinases**; (2) host cell **expressing** systems comprising (I); (3) antibodies to NHP and anti-idiotypic antibodies; (4) fusion proteins comprising NHP; (5) genetically engineered animals that either lack or over **express** (I); (6) antagonists and agonists of NHP; (7) compounds that modulate the **expression** or activity NHP which can be used for diagnosis, drug screening, clinical trial monitoring, treatment of diseases and disorders, and cosmetic or nutriceutical applications; (8) identifying compounds that modulate, **expression** and/or activity of NHP; (9) degenerate nucleic acid variants of (I); (10) vectors that contain (I); (11) nucleotide sequences (e.g. antisense and ribozyme molecules) that inhibit **expression** of (I); and (11) proteins that are functionally equivalent to NHPs.

BIOTECHNOLOGY - Preferred Protein: NHPs are novel proteins **expressed** in **human** cell lines and **human** testis, small intestine, fetal kidney, adenocarcinoma, embryonic carcinoma cells and osteosarcoma cells.

ACTIVITY - Nootropic; Cytostatic.

MECHANISM OF ACTION - Gene therapy. No suitable data given.

USE - NHP oligonucleotides are useful as hybridization probes for screening libraries and assessing gene **expression** patterns. NHP sequences are useful to identify mutations associated with a particular disease and also as a diagnostic or prognostic assay, and also in the molecular mutagenesis/evolution of proteins that are at least partially encoded by the NHP sequences. Sequences derived from regions adjacent to the intron/exon boundaries of NHP gene can be used to design primers for use in amplification assays to detect mutations within the exons, splice sites, introns that can be used in diagnostics and pharmacogenomics. NHP sequences are utilized in microarrays or other assay formats, to screen collections of genetic material from patients who have a particular medical condition. NHP nucleotide sequences are useful for drug screening effective in the treatment of symptomatic or phenotypic manifestations of perturbing the normal function of NHP in the body, and nucleotide constructs encoding NHP products are used to genetically engineer host cells to **express** NHP products *in vivo*. These genetically engineered cells function as bioreactors in the body delivering a continuous supply of a NHP, a NHP peptide, or a NHP fusion protein to the body. Nucleotide construct encoding NHP products are also useful in gene

therapy for modulating NHP **expression** and to produce genetically engineered host cells to **express** NHP products in vivo. NHP nucleotide sequences may also be used as part of ribozyme and/or triple helix sequences that are useful for NHP gene regulation. The encoded NHP polypeptides are useful for generating antibodies, as reagents in diagnostic assays, for identifying other cellular gene products related to NHP and as reagents in assays for screening for compounds that are useful in the treatment of mental, biological or medical disorders and diseases including cancer. (50 pages)

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ACCESSION NUMBER: 2002303299 EMBASE  
TITLE: IL-2 receptor blockade inhibits late, but not early, IFN- $\gamma$  and CD40 ligand **expression** in **human** T cells: Disruption of both IL-12-dependent and -independent pathways of IFN- $\gamma$  production.  
AUTHOR: McDyer J.F.; Li Z.; John S.; **Yu X.**; Wu C.-Y.; Ragheb J.A.  
CORPORATE SOURCE: Dr. J.A. Ragheb, Laboratory of Immunology, National Eye Institute, National Institutes of Health, 10 Center Drive, Bethesda, MD 20892-1857, United States. jr50b@nih.gov  
SOURCE: Journal of Immunology, (1 Sep 2002) 169/5 (2736-2746).  
Refs: 64  
ISSN: 0022-1767 CODEN: JOIMA3  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB mAbs directed against the  $\alpha$ -chain (Tac/CD25) of the IL-2R are an emerging therapy in both transplantation and autoimmune disease. However, the mechanisms underlying their therapeutic efficacy have not been fully elucidated. Therefore, we examined the affect of IL-2R blockade on Th1 and Th2 cytokine production from **human** PBMC. Addition of a humanized anti-Tac Ab (HAT) to activated PBMC cultures inhibited IFN- $\gamma$  production from CD4 and CD8 T cells by 80-90%. HAT partially inhibited production of TNF- $\alpha$  and completely inhibited production of IL-4, IL-5, and IL-10. Furthermore, IL-12, a central regulatory cytokine that induces IFN- $\gamma$ , was undetectable in treated cultures. As T cell-dependent induction of IL-12 is regulated via CD40/CD40 ligand (CD40L) interactions, we examined the affect of HAT on CD40L **expression**. We found CD40L **expression** to be biphasic with an early (6 h) peak that is CD28/IL-2-independent, but a later peak (48 h) being CD28/IL-2-dependent and inhibited by HAT. Similarly, IFN- $\gamma$  production at 6 h was CD28/IL-2-independent but CD28/IL-2-dependent and inhibited by HAT at 48 h. Nonetheless, addition of rCD40L or exogenous IL-12 to HAT-treated cultures could not restore IFN- $\gamma$  production. The IFN- $\gamma$  deficit in such cultures appears to be due to a direct inhibition by HAT of IL-12-independent IFN- $\gamma$  production from T cells rather than altered **expression** of either the IL-12R $\beta$ 1 or IL-12R $\beta$ 2 chains. These data demonstrate that IL-2 plays a critical role in the regulation of Th1 and Th2 responses and impacts both IL-12-dependent and -independent IFN- $\gamma$  production.

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ACCESSION NUMBER: 2002147002 EMBASE  
TITLE: Modulation of p53, ErbB1, ErbB2, and Raf-1 **expression** in lung cancer cells by depsipeptide FR901228.  
AUTHOR: **Yu X.**; Sheng Guo Z.; Marcu M.G.; Neckers L.; Nguyen D.M.; Chen G.A.; Schrump D.S.

CORPORATE SOURCE: Dr. D.S. Schrump, Thoracic Oncology Section, 10 Center Dr., Bethesda, MD 20892-1502, United States  
SOURCE: Journal of the National Cancer Institute, (3 Apr 2002) 94/7 (504-513).  
Refs: 52  
ISSN: 0027-8874 CODEN: JNCIAM  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis  
016 Cancer  
029 Clinical Biochemistry  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Background: Histone deacetylases (HDACs) modulate chromatin structure by regulating acetylation of core histone proteins. HDAC inhibitors, such as depsipeptide FR901228 (FK228), induce growth arrest and apoptosis in a variety of **human** cancer cells by mechanisms that cannot be attributed solely to histone acetylation. This study evaluated the mechanisms by which FK228 mediates apoptosis in non-small-cell lung cancer (NSCLC) cells. Methods: Proliferation and apoptosis were assessed in a panel of NSCLC cell lines that vary in the **expression** of the growth-regulating proteins p53, pRb, and K-Ras treated with a clinically relevant dose of FK228 (25 ng/mL). Western blot and immunoprecipitation techniques were used to analyze **expression** of cell-cycle proteins (cyclin A, cyclin E, p53, and p21), signaling-related proteins (ErbB1, ErbB2, and Raf-1), activity of extracellular signal-regulated **kinase** 1 and 2 (ERK1/2), binding of mutant p53 and Raf-1 to heat shock protein (Hsp)90, and acetylation of Hsp90. Results: FK228 treatment inhibited growth and induced apoptosis in NSCLC cells **expressing** wild-type or mutant p53. FK228 treatment led to altered **expression** of cyclin A, cyclin E, and p21, and to reduced **expression** of mutant, but not wild-type, p53. FK228-treated cells also were depleted of ErbB1, ErbB2, and Raf-1 proteins, and exhibited lower ERK1/2 activity. FK228 treatment also inhibited the binding of mutant p53 and Raf-1 to Hsp90; this inhibition was associated with acetylation of Hsp90. Conclusions: FK228 depletes the levels of several oncoproteins that are normally stabilized by binding to Hsp90 in cancer cells. The resulting ability of FK228 to diminish signal transduction via pathways involving Raf-1 and ERK may contribute to the potency and specificity of this novel antitumor agent.

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ACCESSION NUMBER: 2002286671 EMBASE  
TITLE: Blimp-1 orchestrates plasma cell differentiation by extinguishing the mature B cell gene **expression** program.  
AUTHOR: Shaffer A.L.; Lin K.-I.; Kuo T.C.; **Yu X.**; Hurt E.M.; Rosenwald A.; Giltnane J.M.; Yang L.; Zhao H.; Calame K.; Staudt L.M.  
CORPORATE SOURCE: K. Calame, Department of Microbiology, Columbia Univ. Coll. of Phys./Surg., New York, NY 10032, United States.  
kcl1@columbia.edu  
SOURCE: Immunity, (2002) 17/1 (51-62).  
Refs: 70  
ISSN: 1074-7613 CODEN: IUNIEH  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry  
LANGUAGE: English

SUMMARY LANGUAGE: English

AB Blimp-1, a transcriptional repressor, drives the terminal differentiation of B cells to plasma cells. Using DNA microarrays, we found that introduction of Blimp-1 into B cells blocked **expression** of a remarkably large set of genes, while a much smaller number was induced. Blimp-1 initiated this cascade of gene **expression** changes by directly repressing genes encoding several transcription factors, including Spi-B and Id3, that regulate signaling by the B cell receptor. Blimp-1 also inhibited immunoglobulin class switching by blocking **expression** of AID, Ku70, Ku86, DNA-PKcs, and STAT6. These findings suggest that Blimp-1 promotes plasmacytic differentiation by extinguishing gene **expression** important for B cell receptor signaling, germinal center B cell function, and proliferation while allowing **expression** of important plasma cell genes such as XBP-1.

L16 ANSWER 29 OF 43 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:579538 BIOSIS

DOCUMENT NUMBER: PREV200200579538

TITLE: Development of glucose intolerance in male transgenic mice overexpressing GSK-3beta on a muscle specific promotor.

AUTHOR(S): Pearce, N. J. [Reprint author]; Arch, J. R. S. [Reprint author]; Morrison, A. D. [Reprint author]; Abuin, A. [Reprint author]; Coghlan, M. P. [Reprint author]; Corcoran, S. L. [Reprint author]; Harper, A. J. [Reprint author]; Lister, C. A. [Reprint author]; Llano, A. [Reprint author]; Murphy, G. J. [Reprint author]; Cox, L. Roxbee [Reprint author]; Smith, S. A. [Reprint author]; Taylor, C. M. [Reprint author]; Yates, J. W. [Reprint author]; Holder, J. C. [Reprint author]

CORPORATE SOURCE: GlaxoSmithKline, Harlow, UK

SOURCE: Diabetologia, (August, 2002) Vol. 45, No. Supplement 2, pp. A 70. print.

Meeting Info.: 38th Annual Meeting of the European Association for the Study of Diabetes (EASD). Budapest, Hungary. September 01-05, 2002. European Association for the Study of Diabetes.

CODEN: DBTG AJ. ISSN: 0012-186X.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 13 Nov 2002

Last Updated on STN: 13 Nov 2002

L16 ANSWER 30 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 11

ACCESSION NUMBER: 2002-04068 BIOTECHDS

TITLE: New nucleic acid molecules encoding new **human** proteins, useful in diagnosis, drug screening, clinical trials monitoring, treatment of physiological disorders and cosmetic or nutriceutical applications; vector-mediated **kinase** gene transfer and **expression** in host cell, antibody, DNA probe, DNA primer and transgenic animal for disease diagnosis and gene therapy

AUTHOR: Hu Y; Nepomnichy B; Wang X; Donoho G; Scoville J; **Walke D W**

PATENT ASSIGNEE: Lexicon-Genetics

LOCATION: The Woodlands, TX, USA.

PATENT INFO: WO 2001081557 1 Nov 2001

APPLICATION INFO: WO 2001-US13149 24 Apr 2001

PRIORITY INFO: US 2000-201227 1 May 2000; US 2000-199499 25 Apr 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-034442 [04]

AB A nucleic acid (I) encoding a new **human kinase** (II) with a 1,545 or 1,224 bp DNA sequence fully defined encoding a 514, 407 or 396 amino acid protein sequence fully defined is claimed. Also disclosed as new are: vectors containing (I); host cell containing (I); fusion proteins containing (I); antibodies and anti-idiotype for (I); transgenic animals that lack or overexpress (I); agonist and antagonist of (I); and compounds that modulate the **expression** or activity of (I). (I) gene was isolated by polymerase chain reaction using DNA primers. (I) can be used for diagnosis, drug screening, clinical trial monitoring, physiological disorder therapy and cosmetic or nutriceutical applications. (I) can also be used for gene mapping and as a DNA probe for screening libraries and assessing gene **expression** profiles and for the detection of mutants for disease diagnosis. (I) is also useful in pharmacogenomics. (44pp)

L16 ANSWER 31 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 12

ACCESSION NUMBER: 2002-01107 BIOTECHDS

TITLE: New polynucleotides encoding **human** proteins that share sequence similarity with animals **kinases** e.g. G-protein coupled receptor **kinases**, useful for drug screening, diagnosis and in gene therapy of biological disorders; involving vector-mediated gene transfer for **expression** in host cell, agonist, antagonist, antisense, ribozyme and antibody

AUTHOR: Walke D W; Wilganowski N L; Turner Jr C A

PATENT ASSIGNEE: Lexicon-Genetics

LOCATION: The Woodlands, TX, USA.

PATENT INFO: WO 2001068869 20 Sep 2001

APPLICATION INFO: WO 2001-US7500 8 Mar 2001

PRIORITY INFO: US 2000-188449 10 Mar 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-570872 [64]

AB An isolated nucleic acid molecule (I) comprising a nucleotide sequence encoding new **human** proteins (NHPs), in particular proteins that share sequence similarity with animal **kinases** including G-protein coupled receptor **kinases**, of 553 or 353 amino acids and that hybridizes under stringent conditions to a nucleotide sequence of 1,662 bp or its complement, is claimed. Also claimed is an isolated nucleic acid molecule comprising at least 24 contiguous bases of the sequence. NHP oligonucleotides are useful as hybridization probes for screening libraries and assessing gene **expression** patterns. Sequences derived from regions adjacent to the intron/exon boundaries of NHP gene can be used to design DNA primers that can be used in prognostics, diagnostics and pharmacogenomics. The NHP nucleotide sequences are also useful in drug screening and the nucleotide construct encoding NHP products are useful in gene therapy for modulating NHP **expression**. NHP products can be used to genetically engineer host cells to **express** NHP products *in vivo*, these genetically engineered cells function as bioreactors in the body. NHP sequences are useful in gene **expression** and DNA microarrays. (34pp)

L16 ANSWER 32 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 13

ACCESSION NUMBER: 2001-15821 BIOTECHDS

TITLE: Isolated nucleic acids encoding novel **human** proteins useful for the treatment of disease and as probes for testing and detection; **recombinant kinase** and encoding sense

and antisense DNA for use in therapy and gene therapy and drug screening

AUTHOR: **Walke D W; Hu Y; Nepomnichy B; Turner Jr C A;**

Zambrowicz B

PATENT ASSIGNEE: Lexicon-Genetics

LOCATION: The Woodlands, TX, USA.

PATENT INFO: WO 2001061016 23 Aug 2001

APPLICATION INFO: WO 2001-US5356 15 Feb 2001

PRIORITY INFO: US 2000-184014 22 Feb 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-502793 [55]

AB Isolated nucleic acid molecules (NAMs) encoding new **human** proteins (**kinases**) are claimed. Also claimed are: a NAM (I) having at least 24 contiguous bases of a 3,108 bp sequence or that hybridizes to this sequence under stringent conditions or that encodes a 1,035 amino acid protein sequence (disclosed); NAM (II) comprising a sequence encoding a 1,214 amino acid protein; a NAM (III) having a sequence encoding a 1,007 amino acid protein sequence; a NAM (IV) comprising at least 24 contiguous bases of a 1,007 bp sequence or that hybridizes to it under stringent conditions or that encodes a 576 amino acid sequence; a NAM (V) having a sequence encoding a 560 amino acid sequence; and a NAM (VI) comprising a sequence encoding a 520 amino acid protein sequence. The proteins are mammal transporter proteins useful for therapy and as drug targets for drug discovery. Protein and DNA sequences are disclosed. (I) to (VI) can be used in sense or antisense gene therapy and as probes for diagnosis. Transgenic animals, fusion proteins, antibodies, agonists and antagonists are disclosed. (70pp)

L16 ANSWER 33 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 14

ACCESSION NUMBER: 2001-13012 BIOTECHDS

TITLE: Novel isolated **human** protease polynucleotide that shares structural similarity with animal **kinases** including calcium/calmodulin-dependent protein **kinases** and serine/threonine protein **kinases**, useful in therapeutics; for use in gene therapy

AUTHOR: Donoho G; Scoville J; Turner Jr C A; Friedrich G; Zambrowicz B; **Abuin A**; Sands A T

PATENT ASSIGNEE: Lexicon-Genetics

LOCATION: The Woodlands, TX, USA.

PATENT INFO: WO 2001042435 14 Jun 2001

APPLICATION INFO: WO 2000-US33362 8 Dec 2000

PRIORITY INFO: US 1999-169769 9 Dec 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-381688 [40]

AB An isolated **human** protein-**kinase** (EC-2.7.1.37) polynucleotide (NHP) (I) selected from a polynucleotide comprising at least 24 contiguous bases of a sequence (S) comprising 1,158 bp, a sequence that encodes a 385 or 356 amino acid sequence, and a sequence that hybridizes under stringent conditions to S or its complement, is claimed. (I) is useful in therapeutic, diagnostic and pharmacogenomic applications. (I) is useful for the detection of mutant NHP, or inappropriately **expressed** NHPs for the diagnosis of a disease. (I) is useful for drug screening (or high throughput screening of combinatorial libraries) effective in the treatment of symptomatic or phenotypic manifestations of perturbing the normal function of NHP in the body. (I) is useful in conjunction with polymerase chain reaction to screen libraries, isolate **clones**, and prepare **cloning** and sequencing templates. (I) is useful as hybridization probe for screening libraries, and assessing gene **expression** patterns.

(31pp)

L16 ANSWER 34 OF 43 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN  
DUPLICATE 15

ACCESSION NUMBER: 2001-11030 BIOTECHDS

TITLE: Novel isolated **human kinase**  
polynucleotide useful for screening for drugs effective in  
treatment of symptomatic or phenotypic manifestations of  
perturbing normal function of **human kinase**  
protein in the body;

recombinant protein production via plasmid  
expression in host cell useful in gene therapy

AUTHOR: Mathur B; Turner Jr A C; **Abuin A**; Friedrich G;  
Zambrowicz B; Sands A T

PATENT ASSIGNEE: Lexicon-Genetics

LOCATION: The Woodlands, TX, USA.

PATENT INFO: WO 2001034783 17 May 2001

APPLICATION INFO: WO 2000-US30380 3 Nov 2000

PRIORITY INFO: US 1999-164289 8 Nov 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-335921 [35]

AB An isolated **human kinase** polynucleotide (I) selected  
from a polynucleotide is claimed. (I) contains at least 24 contiguous  
bases of a sequence (S) containing 2,682 bp fully defined, a  
polynucleotide encoding a sequence containing 893 amino acid fully  
defined, and a polynucleotide that hybridizes under stringent conditions  
to (S), or its complement. Also disclosed are: a DNA vector; a  
recombinant host cell; degenerate DNA variants of (I); transgenic  
animals that either lack or over **express** (I); novel  
**human kinase** protein (NHP); (ant)agonists of (I), and  
other compounds that modulate that **expression** or activity of  
(I); a process for identifying (ant)agonists; and antibodies that  
recognize one or more epitopes of a NHP. (I) is useful for detection of  
mutant NHP, or inappropriately **expressed** NHPs for the diagnosis  
of disease. (I) is useful for screening for drugs effective in the  
treatment of symptomatic or phenotypic manifestations of perturbing the  
normal function of NHP in the body. (I) is useful in the molecular  
mutagenesis or evolution of proteins. (I) is useful in conjunction with  
polymerase chain reaction. (I) is useful as a hybridization probe.  
(34pp)

L16 ANSWER 35 OF 43 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:693529 HCAPLUS

DOCUMENT NUMBER: 135:268247

TITLE: Protein and cDNA sequences of novel **human**  
phospholipases homologs and uses thereof in diagnosis,  
therapy and drug screening

INVENTOR(S): Hu, Yi; Nepomnichy, Boris; Donoho, Gregory; Hilbun,  
Erin; Turner, C. Alexander, Jr.; **Abuin**,  
**Alejandro**; Friedrich, Glenn; Zambrowicz, Brian;  
Sands, Arthur T.

PATENT ASSIGNEE(S): Lexicon Genetics Incorporated, USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND  | DATE     | APPLICATION NO. | DATE     |
|---------------|-------|----------|-----------------|----------|
| -----         | ----- | -----    | -----           | -----    |
| WO 2001068871 | A2    | 20010920 | WO 2001-US7994  | 20010313 |

WO 2001068871 A3 20020321  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,  
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2402936 AA 20010920 CA 2001-2402936 20010313  
 US 2002081595 A1 20020627 US 2001-804969 20010313  
 EP 1317551 A2 20030611 EP 2001-920329 20010313  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2004500107 T2 20040108 JP 2001-567355 20010313  
 PRIORITY APPLN. INFO.: US 2000-188885P P 20000313  
 US 2000-189693P P 20000315  
 WO 2001-US7994 W 20010313

AB This invention provides protein and cDNA sequences for newly identified **human** proteins, designated NHPs, which shares structural similarity with animal phospholipases, including phospholipases C  $\delta$ -4. The NHPs are novel proteins that are **expressed** in, *inter alia*, **human** cell lines and **human** fetal and adult brain, cerebellum, spinal cord, thymus, spleen, testis, thyroid, adrenal gland, small intestine, colon, adipose, rectum, and placenta cells. In one embodiment, the invention relates to diagnostic assays for detecting diseases associated with inappropriate NHP activity or levels. Also disclosed are methods for utilizing NHP in drug screening assays and in therapy directed against diseases associated with inappropriate NHP activity or levels.

L16 ANSWER 36 OF 43 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:993521 SCISEARCH

THE GENUINE ARTICLE: 500ZX

TITLE: Relation of gene **expression** phenotype to immunoglobulin mutation genotype in B cell chronic lymphocytic leukemia

AUTHOR: Rosenwald A; Alizadeh A A; Widhopf G; Simon R; Davis R E; **Yu X**; Yang L M; Pickeral O K; Rassenti L Z; Powell J; Botstein D; Byrd J C; Grever M R; Cheson B D; Chiorazzi N; Wilson W H; Kipps T J; Brown P O; Staudt L M (Reprint)

CORPORATE SOURCE: NCI, Metab Branch, Ctr Canc Res, Bldg 10, Rm 4N114, Bethesda, MD 20892 USA (Reprint); NCI, Metab Branch, Ctr Canc Res, Bethesda, MD 20892 USA; Stanford Univ, Sch Med, Dept Biochem, Stanford, CA 94305 USA; Stanford Univ, Sch Med, Dept Genet, Stanford, CA 94305 USA; Stanford Univ, Sch Med, Howard Hughes Med Inst, Stanford, CA 94305 USA; Univ Calif San Diego, Dept Med, La Jolla, CA 92093 USA; NCI, Biometr Res Branch, Div Canc Treatment & Diag, NIH, Bethesda, MD 20892 USA; NIH, Bioinformat & Mol Anal Sect, CBEL, CIT, Bethesda, MD 20892 USA; Walter Reed Army Med Ctr, Dept Med, Washington, DC 20307 USA; Ohio State Univ, Dept Internal Med, Columbus, OH 43214 USA; NCI, CTEP, Div Canc Treatment & Diag, NIH, Bethesda, MD 20892 USA; N Shore Long Isl Jewish Res Inst, Manhasset, NY 11030 USA; NCI, Med Branch, Div Clin Sci, NIH, Bethesda, MD 20892 USA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (3 DEC 2001) Vol. 194, No. 11, pp. 1639-1647.

Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021 USA.

ISSN: 0022-1007.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 29

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The most common **human** leukemia is B cell chronic lymphocytic leukemia (CLL), a malignancy of mature B cells with a characteristic clinical presentation but a variable clinical course. The rearranged immunoglobulin (Ig) genes of CLL cells may be either germ-line in sequence or somatically mutated. Lack of Ig mutations defined a distinctly worse prognostic group of CLL patients raising the possibility that CLL comprises two distinct diseases. Using genomic-scale gene **expression** profiling, we show that CLL is characterized by a common gene **expression** "signature," irrespective of Ig mutational status, suggesting that CLL cases share a common mechanism of transformation and/or cell of origin. Nonetheless, the **expression** of hundreds of other genes correlated with the Ig mutational status, including many genes that are modulated in **expression** during mitogenic B cell receptor signaling. These genes were used to build a CLL subtype predictor that may help in the clinical classification of patients with this disease.

L16 ANSWER 37 OF 43 MEDLINE on STN

ACCESSION NUMBER: 2001464952 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11509132

TITLE: Overexpression of p27(KIP1) induced by Bak gene leads to the arrest in G(1) phase of HCC-9204 cell line.

AUTHOR: Li J; Wang W; **Yu X**; Yang X; Hou Y

CORPORATE SOURCE: Department of Pathology, Fourth Military Medical University, Xin 710033, China.

SOURCE: Zhonghua gan zang bing za zhi = Zhonghua ganzangbing zazhi = Chinese journal of hepatology, (2001 Jul) 9 Suppl 27-9. Journal code: 9710009. ISSN: 1007-3418.

PUB. COUNTRY: China

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Chinese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20010820

Last Updated on STN: 20020122

Entered Medline: 20011204

AB OBJECTIVE: To explore whether p27(KIP1) plays an important role in prolonging cell cycle in G(1) phase and leading to apoptosis of HCC-9204 cells. METHODS: A model of Bak-induced cell cycle arrest in G(1) phase and subsequent apoptosis was established. p27(KIP1) was obtained from the model and sequenced afterwards. A zinc inducible p27(KIP1) stable transfectant was constructed. The effects of inducible p27(KIP1) on cell growth and cell cycle arrest were examined in control pMD and pMD-KIP1 transfected HCC-9204 cells. Western blot was performed to evaluate the **expression** of p27(KIP1). RESULTS: The cell growth was reduced by 35% upon 48h of p27(KIP1) induction with zinc treatment as determined by trypan blue exclusion assay. p27(KIP1) caused cell cycle arrest at 24h after induction, with 40% increase in G(1) population. CONCLUSIONS: Bak may induce cell cycle arrest in G(1) phase through up-regulating **expression** of p27(KIP1). The inducible p27(KIP1)-expressing cells provide a model to assess p27(KIP1) function.

L16 ANSWER 38 OF 43 MEDLINE on STN

ACCESSION NUMBER: 2001106052 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10995753

TITLE: Erythropoietin stimulates proliferation and interferes with differentiation of myoblasts.

AUTHOR: Ogilvie M; **Yu X**; Nicolas-Metral V; Pulido S M;

CORPORATE SOURCE: Liu C; Ruegg U T; Noguchi C T  
Laboratory of Chemical Biology, NIDDK, National Institutes of Health, Bethesda, Maryland 20892-1822, USA.  
SOURCE: Journal of biological chemistry, (2000 Dec 15) 275 (50) 39754-61.  
PUB. COUNTRY: Journal code: 2985121R. ISSN: 0021-9258.  
United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200102  
ENTRY DATE: Entered STN: 20010322  
Last Updated on STN: 20010322  
Entered Medline: 20010208

AB Erythropoietin (Epo) is required for the production of mature red blood cells. The requirement for Epo and its receptor (EpoR) for normal heart development and the response of vascular endothelium and cells of neural origin to Epo provide evidence that the function of Epo as a growth factor or cytokine to protect cells from apoptosis extends beyond the hematopoietic lineage. We now report that the EpoR is **expressed** on myoblasts and can mediate a biological response of these cells to treatment with Epo. Primary murine satellite cells and myoblast C2C12 cells, both of which **express** endogenous EpoR, exhibit a proliferative response to Epo and a marked decrease in terminal differentiation to form myotubes. We also observed that Epo stimulation activates Jak2/Stat5 signal transduction and increases cytoplasmic calcium, which is dependent on tyrosine phosphorylation. In erythroid progenitor cells, Epo stimulates induction of transcription factor GATA-1 and EpoR; in C2C12 cells, GATA-3 and EpoR **expression** are induced. The decrease in differentiation of C2C12 cells is concomitant with an increase in Myf-5 and MyoD **expression** and inhibition of myogenin induction during differentiation, altering the pattern of **expression** of the MyoD family of transcription factors during muscle differentiation. These data suggest that, rather than acting in an instructive or specific mode for differentiation, Epo can stimulate proliferation of myoblasts to expand the progenitor population during differentiation and may have a potential role in muscle development or repair.

L16 ANSWER 39 OF 43 LIFESCI COPYRIGHT 2005 CSA on STN  
ACCESSION NUMBER: 2000:72569 LIFESCI  
TITLE: Activation of Osteocalcin Transcription Involves Interaction of Protein **Kinase** A- and Protein **Kinase** C-dependent Pathways  
AUTHOR: Boguslawski, G.; HaLe, L.V.; **Yu, X.**; Miles, R.R.; Onyia, J.E.; Santerre, R.F.; Chandrasekhar, S.  
CORPORATE SOURCE: Endocrine Division, Lilly Research Laboratories, Indianapolis, Indiana 46285; E-mail: Chandra@lilly.com  
SOURCE: Journal of Biological Chemistry [J. Biol. Chem.], (20000100 vol. 275, no. 2, pp. 999-1006.  
ISSN: 0021-9258.

DOCUMENT TYPE: Journal  
FILE SEGMENT: T; N  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Osteocalcin is a major noncollagenous protein component of bone extracellular matrix, synthesized and secreted exclusively by osteoblastic cells in the late stage of maturation, and is considered indicator of osteoblast differentiation. Osteocalcin **expression** is modulated by parathyroid hormone (PTH) and a variety of other factors. The cAMP-dependent protein **kinase** pathway has been shown previously to have an essential role in PTH signaling and regulation of osteocalcin **expression**. To determine the extent to which other pathways may

also participate in osteocalcin **expression**, we used rat and human osteoblast-like cell lines to generate stably transfected **clones** in which the osteocalcin promoter was fused to a luciferase reporter gene. These **clones** were examined for their responsiveness to agents known to activate or interfere with protein kinase A (PKA)- and protein kinase C (PKC)-dependent pathways. We have found that forskolin, cAMP, and PTH, as well as insulin-like growth factor I (IGF-I) and basic fibroblast growth factor, all were effective in activating the osteocalcin promoter. Phorbol 12-myristate 13-acetate (PMA) was also a strong inducer of the promoter, indicating that PKC plays a role in **expression** of osteocalcin. In combination with PTH or forskolin, the effect of PMA was additive to synergistic. Calphostin C, a selective inhibitor of PKC, decreased the PMA-, PTH-, and IGF-I-induced luciferase activity in a dose-dependent manner; a PKA inhibitor, H-89, also blocked the induction by PTH and IGF-I but not by PMA. We conclude that regulation of osteocalcin transcription is mediated by both PKA-dependent and PKC-dependent mechanisms and that the respective **kinases** reside on a linear or convergent pathway.

L16 ANSWER 40 OF 43 MEDLINE on STN  
ACCESSION NUMBER: 2001554582 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11601053  
TITLE: Gene **expression** of beta-adrenoceptor signal transmitters in heart failure.  
AUTHOR: Yu X; Lin S; Wang X  
CORPORATE SOURCE: Guangdong Provincial Cardiovascular Institute, Guangzhou 510080.  
SOURCE: Zhonghua yi xue za zhi, (1999 Apr) 79 (4) 264-7.  
Journal code: 7511141. ISSN: 0376-2491.  
PUB. COUNTRY: China  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Chinese  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200112  
ENTRY DATE: Entered STN: 20011017  
Last Updated on STN: 20020122  
Entered Medline: 20011205

AB OBJECTIVE: To investigate the alteration in steady-state levels of messenger RNA(mRNA) of beta-adrenoceptor signal transmitters in heart failure. METHODS: The reverse transcription polymerase chain reaction (RT-PCR) was used to assess gene **expression** in small quantity of circulatory lymphocytes. With selected oligonucleotide primers, we used quantitative RT-PCR to amplify mRNAs encoding beta 2-adrenérgic receptor(beta 2-AR), adenylate cyclase (AC), beta 2-adrenergic receptor **kinase**(beta-ARK), and beta-arrestin and cAMP response element binding protein (CREB) in 16 healthy subjects and 30 heart-failing patients. RESULTS: The alteration of gene **expression** in heart failure appeared to be selective, the steady-state levels of mRNA increased significantly involving AC and the transcription factor, CREB; decreased significantly involving membrane receptor, beta 2-AR; unchanged significantly involving phosphorylating factors of beta-AR uncoupling, beta-ARK and beta-arrestin. CONCLUSION: The aberrant gene **expression** of beta-adrenergic receptor might play an important role in the pathogenesis of heart failure.

L16 ANSWER 41 OF 43 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN  
ACCESSION NUMBER: 1999:792357 SCISEARCH  
THE GENUINE ARTICLE: 245HY  
TITLE: A new Drosophila APC homologue associated with adhesive zones of epithelial cells  
AUTHOR: Yu X; Waltzer L; Bienz M (Reprint)  
CORPORATE SOURCE: MRC, MOL BIOL LAB, HILLS RD, CAMBRIDGE CB2 2QH, ENGLAND

COUNTRY OF AUTHOR: (Reprint); MRC, MOL BIOL LAB, CAMBRIDGE CB2 2QH, ENGLAND  
ENGLAND  
SOURCE: NATURE CELL BIOLOGY, (JUL 1999) Vol. 1, No. 3, pp. 144-151

Publisher: MACMILLAN MAGAZINES LTD, PORTERS SOUTH, 4  
CRINAN ST, LONDON N1 9XW, ENGLAND.  
ISSN: 1465-7392.

DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 55

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Adenomatous polyposis coil protein (APC) is an important tumour suppressor in the **human** colon epithelium. In a complex with glycogen synthase **kinase-3** (GSK-3), APC binds to and destabilizes cytoplasmic ('free') beta-catenin. Here, using a yeast two-hybrid screen for proteins that bind to the *Drosophila* beta-catenin homologue, Armadillo, we identify a new *Drosophila* APC homologue, E-APC. E-APC also binds to Shaggy, the *Drosophila* GSK-3 homologue. Interference with E-APC function produces embryonic phenotypes like those of shaggy mutants. Interestingly, E-APC is concentrated in apicolateral adhesive zones of epithelial cells, along with Armadillo and E-cadherin, which are both integral components of the adherens junctions in these zones. Various mutant conditions that cause dissociation of E-APC from these zones also obliterate the segmental modulation of free Armadillo levels that is normally induced by Wingless signalling. We propose that the Armadillo-destabilizing protein complex, consisting of E-APC, Shaggy, and a third protein, Axin, is anchored in adhesive zones, and that Wingless signalling may inhibit the activity of this complex by causing dissociation of E-APC from these zones.

L16 ANSWER 42 OF 43 MEDLINE on STN DUPLICATE 16  
ACCESSION NUMBER: 2000196206 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10447711  
TITLE: Role of mitogen-activated protein **kinases** in activation-induced apoptosis of T cells.  
AUTHOR: Zhu L; **Yu X**; Akatsuka Y; Cooper J A; Anasetti C  
CORPORATE SOURCE: Human Immunogenetics Program, Division of Clinical Research, Fred Hutchison Cancer Research Center, Seattle, WA 98104, USA.  
CONTRACT NUMBER: AI40680 (NIAID)  
CA18029 (NCI)  
CA18221 (NCI)  
+  
SOURCE: Immunology, (1999 May) 97 (1) 26-35.  
PUB. COUNTRY: Journal code: 0374672. ISSN: 0019-2805.  
DOCUMENT TYPE: ENGLAND: United Kingdom  
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)  
FILE SEGMENT: English  
ENTRY MONTH: Priority Journals  
ENTRY DATE: 200004  
Entered STN: 20000413  
Last Updated on STN: 20000413  
Entered Medline: 20000404

AB A member of the mitogen-activated protein (MAP) **kinase** family, Jun N-terminal **kinase** (JNK), has been implicated in regulating apoptosis in various cell types. We have investigated the requirement for another type of MAP **kinase**, extracellular signal-regulated protein **kinase** (ERK) in activation-induced cell death (AICD) of T cells. AICD is the process by which recently activated T cells undergo apoptosis when restimulated through the T-cell antigen receptor. Here we show that both JNK and ERK are activated rapidly upon T-cell receptor (TCR) ligation prior to the onset of AICD. A chemical inhibitor of ERK

activation, PD 098059, inhibits ERK activation and apoptosis, while JNK activation is not inhibited. This suggests that JNK activation is not sufficient for apoptosis. TCR cross-linking induces **expression** of the apoptosis-inducing factor, Fas ligand (FasL), and its **expression** correlates with ERK activation. In addition, apoptosis induced by direct ligation of the Fas receptor by anti-Fas antibody is not associated with ERK activation and is not inhibited by PD 098059. These data suggest that ERK activation is an early event during T-cell apoptosis induced by antigen-receptor ligation, and is not involved in apoptosis per se but in the **expression** of FasL. MAP kinase family members may be similarly involved in inducing apoptosis signals in other cell types.

L16 ANSWER 43 OF 43 MEDLINE on STN DUPLICATE 17  
ACCESSION NUMBER: 1998281583 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9620273  
TITLE: The maize retinoblastoma protein homologue ZmRb-1 is regulated during leaf development and displays conserved interactions with G1/S regulators and plant cyclin D (CycD) proteins.  
AUTHOR: Huntley R; Healy S; Freeman D; Lavender P; de Jager S; Greenwood J; Makker J; Walker E; Jackman M; **Xie Q**; Bannister A J; Kouzarides T; Gutierrez C; Doonan J H; Murray J A  
CORPORATE SOURCE: Institute of Biotechnology, University of Cambridge, UK.  
SOURCE: Plant molecular biology, (1998 May) 37 (1) 155-69.  
Journal code: 9106343. ISSN: 0167-4412.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199806  
ENTRY DATE: Entered STN: 19980708  
Last Updated on STN: 19980708  
Entered Medline: 19980625  
AB Recent discoveries of plant retinoblastoma (Rb) protein homologues and D-type cyclins suggest that control of the onset of cell division in plants may have stronger parallels with mammalian G1/S controls than with yeasts. In mammals, the Rb protein interacts specifically with D-type cyclins and regulates cell proliferation by binding and inhibiting E2F transcription factors. However, the developmental role of Rb in plants and its potential interaction with cell cycle regulators is unknown. We show that the maize Rb homologue ZmRb-1 is temporally and spatially regulated during maize leaf development. ZmRb-1 is highly **expressed** in differentiating cells, but almost undetectable in proliferating cells. In vitro, both ZmRb-1 and **human** Rb bind all classes of plant D-type cyclins with the involvement of a conserved N-terminal Leu-x-Cys-x-Glu (LxCxE) Rb-interaction motif. This binding is strongly reduced by mutation of the conserved Cys-470 of ZmRb-1. ZmRb-1 binds **human** and *Drosophila* E2F, and inhibits transcriptional activation of **human** E2F. We also show that ZmRb-1 is a good in vitro substrate for all **human** G1/S protein **kinases**. The functional conservation of proteins that control the G1/S transition in mammals and plants points to the existence of plant E2F homologues. We conclude that evolution of Rb and cyclin D proteins occurred after separation of the fungi from the higher eukaryotic lineage, but preceded the divergence of plant and animal kingdoms.

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(FILE 'HOME' ENTERED AT 09:20:04 ON 29 MAR 2005)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 09:20:30 ON 29 MAR 2005

L1 1300316 S KINASE?  
L2 484232 S HUMAN AND L1  
L3 6994149 S CLON? OR EXPRESS? OR RECOMBINANT  
L4 241821 S L2 AND L3  
L5 6109328 S CARCINOMA OR BRAIN OR PITUITARY OR KIDNEY  
L6 2104477 S TRACHEA OR LUNG OR SALIVARY OR PROSTATE  
L7 637019 S UMBILICAL (A)VEIN OR AORTA OR ESOPHAGUS OR TONGUE  
L8 55574 S L4 AND L5  
L9 6103 S L4 AND L7  
E YU X/AU  
L10 2286 S E3  
E XIE Q/AU  
L11 709 S E3  
E ABUIN A/AU  
L12 182 S E3-E5  
E WALKE D W/AU  
L13 127 S E3-E6  
L14 3280 S L10 OR L11 OR L12 OR L13  
L15 117 S L4 AND L14  
L16 43 DUP REM L15 (74 DUPLICATES REMOVED)

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| 1  | L1  | 1          | "6734010".pn.  |
| 2  | L2  | 58042      | kinase\$2  |
| 3  | L3  | 47387<br>4 | human  |
| 4  | L4  | 18796      | 12 same 13   |
| 5  | L5  | 71896<br>2 | clon\$3 or express\$3 or recombinant                       |
| 6  | L6  | 10919      | 14 same 15   |
| 7  | L7  | 14381<br>5 | carcinoma or brain or pituitary or kidney                  |
| 8  | L8  | 49097      | (umbilical adj cord)<br>or salivary or prostate or trachea |
| 9  | L9  | 16132<br>5 | 17 or 18   |
| 10 | L10 | 2736       | 16 same 19   |
| 11 | L11 | 2335       | human adj3 12  |
| 12 | L12 | 1229       | 15 same 111  |
| 13 | L13 | 305        | 19 same 112  |
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| 2  | 20050317          | 16           | US<br>20050059101<br>A1 | Bivalent targeting of cell surfaces   |
| 3  | 20050317          | 16           | US<br>20050059101<br>A1 | Bivalent targeting of cell surfaces   |
| 4  | 20050303          | 232          | US<br>20050048490<br>A1 | Proteins associated with cell growth, differentiation, and death  |
| 5  | 20050217          | 81           | US<br>20050037445<br>A1 | Oncology drug innovation  |
| 6  | 20050210          | 38           | US<br>20050032146<br>A1 | Tssk4: a human testis specific serine/threonine kinase  |
| 7  | 20050203          | 90           | US<br>20050026267<br>A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |
| 8  | 20050113          | 35           | US<br>20050009090<br>A1 | Isolated human casein kinase proteins, nucleic acid molecules encoding human casein kinase proteins, and uses thereof |
| 9  | 20050113          | 24           | US<br>20050009019<br>A1 | Tau-opathy model  |
| 10 | 20050106          | 68           | US<br>20050003446<br>A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins and uses thereof                |
| 11 | 20041230          | 69           | US<br>20040266679<br>A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |

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| 13 | 20041209          | 91           | US<br>20040248168<br>A1 | Novel brain-localized protein kinases homologous to homeodomain-interacting protein kinases                    |
| 14 | 20041209          | 125          | US<br>20040248157<br>A1 | Novel polynucleotides encoding soluble polypeptides and methods using same                                     |
| 15 | 20041202          | 678          | US<br>20040241653<br>A1 | Methods for identifying marker genes for cancer  |
| 16 | 20041028          | 47           | US<br>20040214278<br>A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof        |
| 17 | 20041014          | 43           | US<br>20040203127<br>A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof        |
| 18 | 20041014          | 42           | US<br>20040203104<br>A1 | Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof                   |
| 19 | 20041007          | 39           | US<br>20040197930<br>A1 | Proteomic analysis of biological fluids  |
| 20 | 20040923          | 135          | US<br>20040185485<br>A1 | Gene markers useful for detecting skin damage in response to ultraviolet radiation                             |
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| 23 | 20040812          | 102          | US<br>20040157297<br>A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 24 | 20040805          | 53           | US<br>20040152123<br>A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 25 | 20040729          | 102          | US<br>20040146924<br>A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
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| 145 | 20020905   | 63    | US 20020123121 A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 146 | 20020905   | 69    | US 20020123120 A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 147 | 20020829   | 53    | US 20020119548 A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 148 | 20020829   | 94    | US 20020119544 A1 | ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF |
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| 152 | 20020801   | 34    | US 20020103116 A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |
| 153 | 20020801   | 60    | US 20020102691 A1 | Cytokine-, stress-, and oncoprotein-activated human protein kinase kinases  |
| 154 | 20020718   | 69    | US 20020094946 A1 | ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF               |
| 155 | 20020718   | 56    | US 20020094560 A1 | ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF               |
| 156 | 20020711   | 128   | US 20020090624 A1 | Gene markers useful for detecting skin damage in response to ultraviolet radiation                                    |
| 157 | 20020704   | 63    | US 20020086391 A1 | ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF               |
| 158 | 20020627   | 320   | US 20020082189 A1 | ISOLATED HUMAN SERINE/THREONINE KINASE NUCLEIC ACID MOLECULES ENCODING HUMAN SERINE/THREONINE KINASE AND USES THEREOF |
| 159 | 20020620   | 52    | US 20020076783 A1 | Plants and plants cells expressing histidine tagged intimin   |
| 160 | 20020620   | 188   | US 20020076715 A1 | Compositions and methods for ovarian cancer therapy and diagnosis   |
| 161 | 20020613   | 68    | US 20020072491 A1 | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |

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| 162 | 20020606          | 91           | US 20020069426 A1  | Methyl-D-erythritol phosphate pathway genes   |
| 163 | 20020530          | 39           | US 20020064851 A1  | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 164 | 20020509          | 78           | US 20020055160 A1  | ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF |
| 165 | 20020509          | 47           | US 20020055097 A1  | P53-INDUCED APOPTOSIS   |
| 166 | 20020411          | 24           | US 20020042358 A1  | Sphingosine kinase, cloning, expression and methods of use  |
| 167 | 20020411          | 41           | US 20020042101 A1  | Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof            |
| 168 | 20020328          | 70           | US 20020037538 A1  | Compositions, kits, and methods for identification, assessment, prevention, and therapy of psoriasis    |
| 169 | 20020321          | 69           | US 20020034803 A1  | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 170 | 20020321          | 138          | US 20020034780 A1  | Novel human protein kinases and uses therefor   |
| 171 | 20020228          | 40           | US 20020025570 A1  | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 172 | 20020207          | 44           | US 20020015987 A1  | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |

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| 173 | 20011220          | 44           | US 20010053844 A1  | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 174 | 20011213          | 33           | US 20010051360 A1  | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 175 | 20050222          | 75           | US 6858420 B2      | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 176 | 20050208          | 39           | US 6852519 B2      | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 177 | 20050201          | 37           | US 6849420 B2      | Method for determining modulation of p110.delta. activity   |
| 178 | 20050111          | 92           | US 6841717 B2      | Methyl-D-erythritol phosphate pathway genes   |
| 179 | 20041228          | 60           | US 6835562 B2      | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |
| 180 | 20041214          | 22           | US 6830916 B2      | Sphingosine kinase, cloning, expression and methods of use  |
| 181 | 20041214          | 45           | US 6830912 B2      | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins and uses thereof  |
| 182 | 20041214          | 39           | US 6830911 B2      | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof |

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| 183 | 20041123 | 179 | US 6821765<br>B2 | Isolated human kinase<br>proteins, nucleic acid<br>molecules encoding human<br>kinase proteins, and<br>uses thereof |
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| 184 | 20041102          | 65           | US 6812014<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins and uses thereof                |
| 185 | 20041026          | 37           | US 6808912<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |
| 186 | 20041026          | 86           | US 6808911<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |
| 187 | 20041019          | 73           | US 6806072<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |
| 188 | 20041005          | 50           | US 6800471<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |
| 189 | 20041005          | 41           | US 6800470<br>B2   | Mammalian sphingosine kinase type 2 isoforms, cloning, expression and methods of use thereof                          |
| 190 | 20041005          | 32           | US 6800283<br>B2   | Isolated human casein kinase proteins, nucleic acid molecules encoding human casein kinase proteins, and uses thereof |
| 191 | 20040921          | 109          | US 6794137<br>B2   | Gene markers useful for detecting skin damage in response to ultraviolet radiation                                    |
| 192 | 20040824          | 87           | US 6780626<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof               |

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| 193 | 20040810          | 16           | US 6774226<br>B1   | Isolated nucleic acid molecules encoding cancer associated antigens, the antigens per se, and uses thereof |
| 194 | 20040622          | 98           | US 6753175<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof    |
| 195 | 20040525          | 81           | US 6740513<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof    |
| 196 | 20040511          | 50           | US 6733978<br>B2   | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof    |
| 197 | 20040504          | 96           | US 6730506<br>B2   | Isolated human kinase proteins   |
| 198 | 20040504          | 60           | US 6730480<br>B1   | Sphingosine kinase enzyme  |
| 199 | 20040427          | 38           | US 6727066<br>B2   | Genes expressed in treated human C3A liver cell cultures   |
| 200 | 20040406          | 59           | US 6716604<br>B2   | Nucleic acid molecules encoding a subunit of a human calcium/calmodulin-dependent protein kinase           |
| 201 | 20040316          | 106          | US 6706511<br>B2   | Isolated human kinase proteins   |

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| 3  | 20041209   | 91    | US<br>20040248168<br>A1 | Novel brain-localized protein kinases homologous to homeodomain-interacting protein kinases |
| 4  | 20040708   | 58    | US<br>20040132053<br>A1 | Sphingosine kinase enzyme   |
| 5  | 20040527   | 56    | US<br>20040101857<br>A1 | Modulation of cytokine-inducible kinase expression  |
| 6  | 20040513   | 78    | US<br>20040092469<br>A1 | Androgen-regulated PMEPA1 gene and polypeptides   |
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| 11 | 20040115   | 45    | US<br>20040009935<br>A1 | Antisense modulation of p21-activated kinase 2 expression                                   |
| 12 | 20031127   | 103   | US<br>20030220224<br>A1 | Novel polynucleotides encoding the human citron kinase polypeptide, BMSNKC_0020/0021        |
| 13 | 20031113   | 136   | US<br>20030211093<br>A1 | Human kinases   |
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| 17 | 20021226   | 179   | US 20020198362 A1 | Compositions and methods for the detection, diagnosis and therapy of hematological malignancies   |
| 18 | 20021114   | 345   | US 20020168711 A1 | Nucleic acids, proteins, and antibodies   |
| 19 | 20020509   | 47    | US 20020055097 A1 | P53-INDUCED APOPTOSIS   |
| 20 | 20041214   | 39    | US 6830911 B2     | Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof                                     |
| 21 | 20040504   | 60    | US 6730480 B1     | Sphingosine kinase enzyme   |
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| 23 | 20030520   | 58    | US 6566130 B1     | Androgen-regulated gene expressed in prostate tissue  |
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| 27 | 19991228          | 27           | US 6007991 A       | Antisense oligonucleotides for mitogen-activated protein kinases as therapy for cancer |